IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF NEW YORK

REGENERON PHARMACEUTICALS, INC. Plaintiff, v. NOVARTIS PHARMA AG, NOVARTIS TECHNOLOGY LLC, NOVARTIS PHARMACEUTICALS CORPORATION, VETTER PHARMA INTERNATIONAL GMBH Defendants.	CASE NO.: JURY TRIAL DEMANDED **COMPLAINT**

Plaintiff Regeneron Pharmaceuticals, Inc. ("**Regeneron**") files this Complaint against Defendants, Novartis Pharma AG, Novartis Technology LLC, and Novartis Pharmaceuticals Corporation (collectively, "**Novartis**") and Vetter Pharma International GmbH ("**Vetter**"), and alleges, upon knowledge as to itself and otherwise upon information and belief, as follows:

NATURE OF ACTION

1. Plaintiff Regeneron's EYLEA® (aflibercept) injection ("**EYLEA**") is an innovative biologic drug for the treatment of a variety of severe eye diseases.

2. Defendant Novartis developed and recently launched BEOVU® (brolucizumab-dbll) injection ("**BEOVU**"), which competes against EYLEA to treat a certain eye disease. Novartis, together with Genentech, Inc. ("**Genentech**"), also co-developed LUCENTIS® (ranibizumab) injection ("**LUCENTIS**"), which competes against EYLEA to treat most of the same eye diseases. Novartis markets LUCENTIS outside of the United States, and benefits from the sales of LUCENTIS in the United States through its significant financial stake in Roche

Holding AG ("**Roche**"), the parent company of Genentech, which markets LUCENTIS in the United States.[1] Defendant Vetter is an essential supply chain provider of drug "filling" services and is the exclusive filler for Novartis's LUCENTIS prefilled syringe ("**PFS**") product. Upon information and belief, Vetter will be the filler for Novartis's BEOVU PFS once it launches in the United States. Vetter also has a longstanding relationship with Regeneron, both as a filler for EYLEA vials and as a prior development partner for an EYLEA PFS.

3. Defendant Novartis, unwilling to compete on the clinical merits of LUCENTIS or BEOVU against EYLEA, has done everything in its power to try to stop EYLEA through anticompetitive means. BEOVU's launch has been riddled with serious safety issues, and LUCENTIS is a less effective treatment than EYLEA for certain diabetic eye diseases ***and*** requires more frequent injections (per the FDA-approved label) at a time when in-patient trips to medical doctors are difficult with the COVID-19 pandemic.[2] Novartis has therefore resorted to various unlawful means, including the enforcement of a fraudulently procured United States patent and an anticompetitive licensing and settlement agreement with Vetter, all as part of a scheme to attempt to monopolize the market and/or unreasonably restrain competition for PFS ophthalmic drug treatments. Defendants' purpose and intent throughout this scheme has been to prevent, deter, or at least delay the competitive launch of EYLEA PFS for years, to artificially inflate Regeneron's costs of entry, and now to stop Regeneron altogether from competing in the U.S. market with

[1] All references to LUCENTIS refer to the product that was co-developed by Novartis and is marketed by Novartis outside the United States and by Genentech inside the United States.

[2] *Compare* U.S. Food and Drug Administration, Lucentis® (ranibizumab injection), "Highlights of Prescribing Information, *available at* https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/125156s111lbl.pdf *with* U.S. Food and Drug Administration, Eylea® (aflibercept), "Highlights of Prescribing Information, *available at* https://www.regeneron.com/sites/default/files/EYLEA_FPI.pdf.

EYLEA PFS. In addition to Regeneron, physicians and patients have been the victims of this scheme because Novartis's and Vetter's actions are aimed at limiting the availability of the most effective and convenient ophthalmic PFS drug treatment—EYLEA PFS.

4. By this action for injunctive relief and damages, Regeneron seeks to stop Defendants Novartis and Vetter from continuing their illegal conduct in violation of Sections 1 and 2 of the Sherman Antitrust Act, 15 U.S.C. §§ 1 and 2.

INTRODUCTION

5. Regeneron's EYLEA and Novartis's LUCENTIS and BEOVU are competing drugs that treat certain eye diseases involving overproduction of a naturally occurring protein in the body called vascular endothelial growth factor ("**VEGF**"). This VEGF overproduction can cause vision loss and even blindness, and many millions of patients suffer from VEGF-related eye diseases.

6. As "anti-VEGF" drugs, EYLEA, LUCENTIS, and BEOVU must be injected with regular frequency into a patient's eye. The frequency, manner, and safety of injection are important factors in the success of treatment, and the method of administration is therefore significant. In that regard, EYLEA and LUCENTIS were historically sold only in vial form and ultimately loaded into a separate needle or syringe for injection. Recently, however, the market for anti-VEGFs has converted from vial to PFS, which is a more accurate and more convenient method of administration that carries a lower risk of introducing foreign particles into the eye, which can cause severe complications such as endophthalmitis. LUCENTIS and EYLEA are by far the primary approved anti-VEGF PFS available in the United States.[3]

7. There are numerous challenges associated with commercializing a PFS with a

[3] While Macugen received FDA approval in 2004 for a prefilled syringe to treat one VEGF-related eye disease only, it is also an older, less effective treatment that is rarely prescribed anymore, if at all.

complex biologic drug such as EYLEA or LUCENTIS. For example, there are a limited number of companies that can fill the syringe with the drug in accordance with the required sterile conditions, and the existing "fillers" have limited capacity. Vetter is the leading PFS filler and is the exclusive PFS filler for Novartis's LUCENTIS PFS. Regeneron and Vetter also have had a long-standing relationship. For many years, Vetter has provided non-exclusive filling services to Regeneron for EYLEA in vial form. More specifically, starting in 2005, Regeneron and Vetter also embarked on a collaboration to commercialize an EYLEA PFS. This successful collaboration led to regulatory approval for EYLEA PFS in Australia in 2012.

8. Unbeknownst to Regeneron, however, as Regeneron and Vetter were jointly working to commercialize an EYLEA PFS, Novartis was pursuing its own mission in 2013 to fraudulently procure a United States patent claiming a PFS containing ***any*** anti-VEGF drug, including EYLEA, which Novartis and Vetter would soon use to unreasonably restrain Regeneron's ability to compete. Given that the prior art already described and disclosed such a PFS, Novartis could secure its patent only by ensuring that the U.S. Patent and Trademark Office ("**USPTO**") was not aware of that prior art. And Novartis did just that. By ***deliberately*** withholding material prior art from the USPTO, Novartis succeeded in obtaining a patent—U.S. Patent No. 9,220,631 (the "**'631 Patent**")—broadly claiming a PFS with ***any anti-VEGF***, including EYLEA.[4] As pled in detail below, specific Novartis employees involved in the prosecution of the '631 Patent knew of the omitted prior art and also knew the omitted prior art was material because of multiple decisions by a set of USPTO examiners in a separate patent application covering overlapping subject matter that Novartis ultimately abandoned. In order to gain allowance of the '631 Patent, the Novartis employees made a deliberate decision to withhold the prior art from the ***different***

[4] The '631 Patent specifically identifies EYLEA and states that "[a]flibercept is the preferred non-antibody VEGF antagonist for use with the invention." '631 Patent at Col. 6, ll. 42-43.

USPTO examiner that was reviewing the application for the ’631 patent.

9. Further unknown to Regeneron, Novartis and Vetter were vying to control the patent application underlying the ’631 Patent. Using this dispute as a pretense, Novartis and Vetter entered into an anticompetitive conspiracy around 2013 to unreasonably restrain competition in anti-VEGF PFS treatments for ophthalmic diseases. Novartis effectively used the settlement process for the then-pending application that would become the ’631 Patent to obtain control and influence over Vetter’s PFS filling services so as to inhibit anti-VEGF rivals like Regeneron. This “settlement” provided Vetter with a “co-exclusive” license to what would become Novartis’s fraudulently procured ’631 Patent and the exclusive right to grant sublicenses. The *quid pro quo* was that Novartis extracted a lucrative economic interest in Vetter’s PFS filling services in the form of Vetter’s assent to place onerous and anticompetitive restrictions on Novartis’s rivals—like Regeneron—that had been working with Vetter all along. This anticompetitive agreement co-opted Vetter and enabled Novartis to exert influence over Vetter’s current and future customer relationships so that Novartis could undermine competitors’ efforts to develop and sell competing anti-VEGF PFS drugs. As for Vetter, it stood to benefit from this agreement by becoming the sole filler for all anti-VEGF PFS drugs—since Novartis would wield its fraudulently procured ’631 Patent against any company that tried to compete by using a different PFS filler.

10. Immediately following its “settlement” with Novartis, and despite the approximately eight year long collaboration with Regeneron to commercialize an EYLEA PFS, Vetter did just as Novartis had intended. Vetter abruptly reversed course with Regeneron in 2013. Vetter chose the path of illicit profits by colluding with Novartis to control the supply of anti-VEGF PFS treatments. Specifically, Vetter contacted Regeneron in October 2013, claimed that Novartis had a pending patent application, and demanded that Regeneron take a sublicense to the

yet to be issued '631 Patent before Vetter would continue their collaboration on EYLEA PFS—***even though the '631 Patent would not even issue for two more years***. As a condition of continuing their work on EYLEA PFS, Vetter also required that Regeneron submit to two anticompetitive restrictions: (1) Regeneron must use Vetter as its exclusive PFS filler for the next 20 years—*i.e.*, for the entire life of Novartis's yet to be issued '631 Patent; and (2) Regeneron must never challenge the validity or enforceability of Novartis's yet to be issued '631 Patent.

11. Regeneron could not—and did not—accept this offer. First, the unlawful "no challenge" requirement was unacceptable given Regeneron's own role in developing EYLEA PFS and the extensive prior art (including the prior art Novartis deliberately withheld from the USPTO during prosecution of the '631 Patent) showing that the claimed PFS in Novartis's patent was not patentable. Separately, Regeneron could not agree to be locked into an exclusive supply arrangement with Vetter for 20 years because it would inhibit the competitiveness of EYLEA PFS. Vetter is the capacity-constrained exclusive supplier of LUCENTIS PFS and Regeneron had certain quality concerns about Vetter as its sole PFS filler—two issues that Vetter failed to address. Consequently, Regeneron had no choice but to decline Vetter's (and Novartis's) unlawful demands.

12. The overarching goal of Novartis's and Vetter's conspiracy has been to control—and unreasonably restrain—competition in anti-VEGF PFS treatments for certain ophthalmic diseases. Their initial plan was to have all anti-VEGF PFS drugs run through Novartis and the PFS filling services for those drugs to run exclusively through Vetter. Regeneron's EYLEA has been the only real competitive threat to LUCENTIS PFS, giving both Novartis and Vetter (now as a co-conspirator) significant economic motives to lock up Regeneron's EYLEA PFS business by leveraging Novartis's fraudulently procured '631 Patent. To this end, Novartis and Vetter sought

to hold Regeneron captive to Vetter's limited-supply PFS filling services for 20 years as a condition of Regeneron obtaining a covenant that Novartis (or Vetter) would not sue Regeneron on the fraudulently procured '631 Patent. But when Regeneron rejected Novartis's and Vetter's unlawful efforts to coerce Regeneron into an exclusive arrangement, Novartis and Vetter conspired to keep EYLEA PFS out of the market altogether.

13. To Novartis's benefit, Novartis and Vetter agreed to deny Regeneron access to ***any*** of Vetter's essential PFS filling services for EYLEA PFS. Not only did this denial represent an abrupt change in Vetter's collaboration with Regeneron to commercialize EYLEA PFS, but it also was in stark contrast to Vetter's then and current relationship with Regeneron filling EYLEA vials ***without*** exclusivity. As for commercialization of the EYLEA PFS, Novartis and Vetter knew that Regeneron would need to start over with few to no PFS filler options for this critical aspect of the supply chain, resulting in years of delay and additional, substantial, and unnecessary costs. And that is exactly what happened to Regeneron.

14. Novartis and Vetter did not stop there, however. They doubled down on their conspiracy to limit competition from EYLEA PFS after the '631 Patent issued in December 2015. With the fraudulently procured '631 Patent in hand by that point, Vetter again demanded the same anticompetitive terms (an exclusive filling agreement and no challenge clause) from Regeneron in late 2017. Regeneron again refused. Two and a half years later, after Regeneron had successfully created a new supply and filler chain for EYLEA PFS and launched it in the United States, and when Novartis's BEOVU's safety problems came to light, Novartis took the next step in this illicit scheme. On June 19, 2020, Novartis filed a patent infringement complaint at the U.S. International Trade Commission ("**ITC**") asserting its fraudulently procured '631 Patent and seeking an exclusion order barring importation of EYLEA PFS components into the United States. Novartis

also filed a companion infringement complaint in the Northern District of New York ("NDNY") seeking damages and injunctive relief for alleged infringement of '631 Patent. Despite knowing that the '631 Patent was fraudulently procured and unenforceable, Novartis filed multiple litigations in yet another attempt to block EYLEA PFS from the U.S. market, or at the very least, to artificially increase Regeneron's costs even more by erecting anticompetitive barriers to sale.

15. Defendants' anticompetitive conduct has injured and continues to injure patients, physicians, and Regeneron. Instead of competing on the merits, Novartis and Vetter have concocted numerous anticompetitive obstacles to initially try to stop Regeneron from launching—and now from selling—EYLEA PFS. By forcing Regeneron to navigate around artificial and unlawful barriers, Defendants have delayed EYLEA PFS by years in coming to the U.S. market. Defendants imposed additional, substantial, and unnecessary costs on Regeneron to establish a reliable alternative supply and filler chain in order to commercialize EYLEA PFS. Now Defendants are forcing Regeneron to spend time and limited resources defending an ITC action and a patent infringement lawsuit based on a fraudulently procured patent, and would have Regeneron invest millions of dollars and months attempting to develop a contingent supply of EYLEA in vial form to hedge against the possibility that Novartis obtains an exclusion order from the ITC.

16. Worst of all, if Novartis's unlawful efforts succeed, patients and physicians will be deprived of EYLEA PFS altogether. Novartis will regain its monopoly over anti-VEGF PFS treatments for ophthalmic diseases and Vetter will remain the sole PFS filler for those treatments. Tellingly, in its ITC submissions, Novartis does not even attempt to claim that any alternative anti-VEGF PFS exists for EYLEA PFS other than LUCENTIS PFS. And the only other potential near-term PFS entrant is another Novartis drug, BEOVU, which has serious safety issues. Through the

anticompetitive enforcement of the fraudulently procured '631 Patent, Novartis is trying to force physicians and patients to make a difficult choice between LUCENTIS PFS, which offers numerous advantages through its PFS delivery method, and the EYLEA vial, a medication that is regarded by many physicians and patients as a superior anti-VEGF eye disease treatment but is administered using a non-preferred method. This is particularly harmful because physicians are naturally reluctant to switch a patient who is responding well to one anti-VEGF to another anti-VEGF treatment. In a competitive marketplace, physicians and patients would not have to make this difficult tradeoff. They should continue to have access to an anti-VEGF PFS that combines all of these medical advantages in one—Regeneron's EYLEA PFS.

17. Regeneron is compelled to bring this lawsuit to stop Defendants' unlawful behavior and to hold Defendants accountable in front of a jury in a public court of law for their anticompetitive conduct.

PARTIES TO ACTION

18. Plaintiff Regeneron is a corporation organized and existing under the laws of the State of New York with its principal place of business located at 777 Old Saw Mill River Road, Tarrytown, New York 10591. Regeneron is in the business of inventing, developing, manufacturing, and marketing a variety of innovative pharmaceutical products, including EYLEA and EYLEA PFS.

19. Defendant Novartis Pharma AG is a corporation organized and existing under the laws of Switzerland, with an office and a place of business located at Forum 1 Novartis Campus, CH-4056 Basel, Switzerland.

20. Defendant Novartis Pharmaceuticals Corporation is a corporation organized and existing under the laws of the state of Delaware with its principal place of business located at One

Health Plaza, East Hanover, New Jersey 07936. Novartis Pharmaceuticals Corporation is an affiliate of Novartis Pharma AG.

21. Defendant Novartis Technology LLC is a corporation organized and existing under the laws of the state of Delaware with its principal place of business located at One Health Plaza, East Hanover, New Jersey 07936.

22. Defendant Vetter is a company organized and existing under the laws of Germany, with its principal place of business located at Eywiesenstrasse 5, 88212 Ravensburg, Germany. Vetter also operates facilities located in Des Plaines and Skokie, Illinois.[5]

JURISDICTION AND VENUE

23. This Court has subject matter jurisdiction over all claims asserted against Defendants pursuant to 28 U.S.C. § 1331, 28 U.S.C. § 1337(a), 15 U.S.C. § 4, 15 U.S.C. § 15, and 15 U.S.C. § 26.

24. This Court has personal jurisdiction over Defendants under the U.S. Constitution and nationwide contacts under Section 12 of the Clayton Act, 15 U.S.C. § 22.

25. Venue is proper in this District under Section 12 of the Clayton Act, 15 U.S.C. § 22, and under 28 U.S.C. § 1391(b) and (c).

26. For personal jurisdiction and venue purposes, Defendants can be found in, and transact business in, this District, including through the marketing and sale of LUCENTIS PFS and BEOVU. Defendants' unlawful behavior was specifically intended to, has had, and will continue to have an anticompetitive effect and impact on Regeneron and U.S. consumers in this District, and elsewhere.

[5] Vetter U.S. Locations, *available at* https://www.vetter-pharma.com/en/about-us/locations/chicago-skokie (last visited July 11, 2020).

INTERSTATE COMMERCE

27. The commercialization, development, manufacturing, marketing, sale, and distribution of EYLEA, LUCENTIS, and BEOVU occurs in interstate commerce.

FACTUAL BACKGROUND[6]

A. Anti-VEGF Drugs for Treating Ophthalmic Diseases

28. Anti-VEGF drugs, like EYLEA and LUCENTIS, are used to treat certain ophthalmic diseases that can cause vision loss or blindness, including Wet Age-Related Macular Degeneration, Diabetic Retinopathy, Diabetic Macular Edema, and Macular Edema following Retinal Vein Occlusion. Another anti-VEGF drug, BEOVU, was recently approved for the treatment of Wet Age-Related Macular Degeneration only.

29. These complex biologics work by targeting over-produced VEGF proteins and blocking or inhibiting them. This reduces abnormal blood vessel growth and leakage in the eye, which helps to stabilize vision loss, and in some cases, can even reverse vision loss and restore sight. Anti-VEGF treatments are only effective at maintaining or improving vision when administered regularly on a continuing basis.

30. Patients receive treatment for these ophthalmic diseases in a physician's office. An ophthalmologist (typically a retinal specialist) must administer anti-VEGF drugs via syringe with an injection near the retina in the back of the eye, known as an "intravitreal injection."

B. Ophthalmic Diseases that Cause Vision Loss and Blindness

i. Wet Age-Related Macular Degeneration

31. Wet Age-Related Macular Degeneration ("**wet AMD**") is the most severe form of

[6] The factual allegations in this Complaint are made based upon Regeneron's first-hand knowledge with the exception of allegations made upon information and belief regarding Defendants' conduct.

an eye disease that is the leading cause of blindness among older Americans.

32. An estimated 11 million Americans suffer from some form of AMD, which erodes central vision. AMD has two forms: wet and dry. While dry AMD leads to a gradual loss of vision, wet AMD leads to faster vision loss and is the most advanced form of the disease. It is responsible for 90 percent of all AMD-related blindness.

33. Wet AMD patients see the world as if through distorted lenses: straight lines may appear bent, central vision may be reduced, colors may be dulled, and patients may see haziness. Patients may also experience a well-defined blurry or blind spot in their central field of vision:[7]

34. Day-to-day activities, such as reading, writing, driving, or even recognizing faces, are difficult for patients with wet AMD. The debilitating effects of wet AMD worsen over time and can be irreversible. If left untreated, wet AMD may cause permanent blindness.

35. Wet AMD is caused by an overproduction of a naturally occurring VEGF protein in the body. VEGF's normal role is to trigger formation of new blood vessels supporting the growth of the human body's tissues and organs. When cells secrete too much VEGF into the eye, however, abnormal blood vessels grow underneath the macula and retina. These abnormal blood vessels can leak blood or fluid, blurring central vision and potentially causing blindness.

[7] National Institutes of Health, https://www.nih.gov/health-information/nih-clinical-research-trials-you/age-related-macular-degeneration-amd (last visited July 13, 2020).

ii. Diabetic Retinopathy and Diabetic Macular Edema

36. Diabetes is the leading cause of new cases of blindness in people 20 to 74 years of age in the United States.

37. Diabetic Retinopathy ("**DR**") is the most common diabetic eye disease and can lead to vision loss. DR occurs when too much blood sugar damages the blood vessels in the retina. As a result, the retina does not receive enough oxygen and nutrients, and blood vessels can leak blood and fluid into the retina.

38. If DR progresses into its most advanced stage, an increased growth of new blood vessels occurs. These new blood vessels are fragile and easily damaged, which adds to the swelling and leaking in the retina.

39. Diabetic Macular Edema ("**DME**") is a complication of DR that can lead to further vision problems. DME occurs if the macula, the area of the retina at the back of the eye responsible for sharp central vision, swells with fluid leaked from those damaged blood vessels. DME can degrade the patient's vision and, if left untreated, can cause blindness.

iii. Macular Edema following Retinal Vein Occlusion

40. Retinal Vein Occlusion ("**RVO**") occurs when a blood vessel in the retina becomes blocked, often by a blood clot.

41. When fluid leaks into the macula as a result of the blocked blood vessel, it is called Macular Edema following Retinal Vein Occlusion ("**MEfRVO**"). Vision loss or blurring occurs as the macula swells with the fluid.

C. FDA-Approved Anti-VEGF Drugs

42. There are several anti-VEGFs approved by the U.S. Food and Drug Administration ("**FDA**") to treat certain ophthalmic diseases in the United States. The two primary approved drug treatments include EYLEA and LUCENTIS. Recently, FDA approved another anti-VEGF drug

product for the treatment of wet AMD, BEOVU® (brolucizumab-dbll) injection. BEOVU is also marketed by Defendant Novartis, but it has resulted in a host of severe safety issues for patients.

i. LUCENTIS

43. LUCENTIS is the brand name for the anti-VEGF (ranibizumab injection) co-developed by Defendant Novartis and Genentech, a wholly-owned subsidiary of Roche. Novartis paid Genentech/Roche an initial milestone fee and shared the cost for the subsequent development by making additional milestone payments upon the achievement of certain clinical development points and product approval. Novartis also markets and pays royalties on the net sales of LUCENTIS outside of the United States.[8]

44. FDA first approved LUCENTIS in vial form in the United States in June 2006. FDA approved LUCENTIS in a PFS in October 2016, and it launched shortly thereafter in early 2017. At this time nearly all LUCENTIS is sold in PFS in the United States.

45. LUCENTIS is currently indicated for the treatment of patients with certain ophthalmic diseases, including wet AMD, DR, DME, and MEfRVO. LUCENTIS is recommended for intravitreal injection once a month.

46. LUCENTIS is a multi-billion dollar franchise globally. LUCENTIS sales in the United States in 2018 amounted to approximately $1.6 billion[9] while LUCENTIS sales in Europe

[8] Form 20-F 2009, Novartis AG, "United States Securities and Exchange Commission Form 20-F 2009" (Jan. 26, 2010), *available at* https://www.novartis.com/sites/www.novartis.com/files/Novartis-20-F-2009.pdf.

[9] Finance Report 2018, Roche, "Finance Report 2018" *available at* https://www.roche.com/dam/jcr:933329c4-4564-4b17-a29b-246ac7e617d5/en/fb18e.pdf (last visited July 13, 2020).

and the rest of the world in 2018 amounted to $2 billion.[10]

47. Under the terms of their commercial agreement, Genentech has marketing rights for LUCENTIS in North America (United States, Canada, and Mexico) while Novartis has exclusive commercialization rights to sell LUCENTIS in Europe and the rest of the world.[11]

48. Novartis has multiple economic interests in the LUCENTIS franchise. Novartis not only has 100% of the commercial rights for LUCENTIS outside of North America, but it also owns a 33.3% stake in Roche—the parent company of Genentech that sells LUCENTIS PFS in the United States. Novartis has had an ownership in Roche dating back to 2001.[12] Indeed, Novartis's current 33.3% stake in Roche is worth approximately $12.9 billion.[13] Novartis has received dividend payments from Roche in excess of CHF 4 billion (approximately $4.3 billion USD) since 2001.[14] Novartis accordingly benefits from LUCENTIS' sales outside of the U.S. as well as LUCENTIS' U.S. sales through its 33.3% ownership stake in Roche.

49. In addition, Novartis licensed its '631 Patent to Genentech for LUCENTIS PFS in the United States.[15] According to Novartis, the "LUCENTIS PFS uses Novartis's PFS technology

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[10] Form 20-F 2018, Novartis AG, "United States Securities and Exchange Commission Form 20-F 2018" (Jan. 30, 2019), *available at* https://www.novartis.com/sites/www.novartis.com/files/novartis-20-f-2018.pdf.

[11] Press Release, Genentech, "Genentech and Novartis Ophthalmics Announce Development and Commercialization Agreement for Age-Related Macular Degeneration Treatment, Lucentis" (June 24, 2003), *available at* https://www.gene.com/media/press-releases/6327/2003-06-24/genentech-and-novartis-ophthalmics-annou.

[12] Roche, Investors, Frequently Asked Questions, Major Shareholders, *available at* https://www.roche.com/investors/faq_investors/major_shareholders.htm (last visited July 13, 2020).

[13] Novartis, 2018 Annual Report, *available at* https://www.novartis.com/sites/www.novartis.com/files/novartis-annual-report-2018-en.pdf.

[14] *Novartis Delays Sale of Roche Stake*, SeeNews Switzerland (Oct. 24, 2016), *available at* https://advance.lexis.com/api/permalink/8b30d1d6-ccfd-4f0d-bed0-1c5bd7708fee/?context=1000516.

[15] *See Certain Pre-Filled Syringes for Intravitreal Injection and Components Thereof*, DN 3460,

including the inventions recited in the '631 patent. Genentech's commercialization of the LUCENTIS PFS in the United States is pursuant to a license to that technology, including the '631 [P]atent."[16]

ii. EYLEA

50. EYLEA (aflibercept) is a novel and groundbreaking anti-VEGF developed by Regeneron. EYLEA is an entirely different biologic than LUCENTIS. EYLEA is currently indicated for the treatment of patients with the following ophthalmic diseases: wet AMD, DR, DME, and MEfRVO.

51. Regeneron's EYLEA provides substantial benefits to patients compared to LUCENTIS because it requires less frequent injections. EYLEA is recommended for intravitreal injection once a month for the first three months, but then—unlike LUCENTIS—EYLEA can be injected once every two months to treat wet AMD, DR, and DME. Clinical studies show that EYLEA administered every two months was clinically equivalent to LUCENTIS (the previous standard of care) dosed every month.[17] EYLEA also has been proven to provide superior vision gains when compared to treatment with LUCENTIS in certain patients with DME.[18]

52. Because of its unique design (wherein two VEGF-binding domains from two

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USITC No. 337-TA-[__], Compl., ¶ 7 (June 19, 2020) ("Additionally, Novartis licensed the '631 patent to Genentech, Inc. ('Genentech'). Genentech operates an industry in the United States relating to the Asserted Patent based on its LUCENTIS® (ranibizumab) pre-filled syringe product ("LUCENTIS PFS"), which practices at least one claim of the Asserted Patent."); ¶ 14 ("Genentech is licensed by Novartis to practice the Asserted Patent and is the exclusive U.S. provider of the LUCENTIS PFS, a domestic industry product.") (the "ITC Compl.").

16 *See* ITC Compl., ¶ 29.

17 *Id.*

18 *See* Wells, "Aflibercept, Bevacizumab, or Ranibizumab for Diabetic Macular Edema: Two-year Results from a Comparative Effectiveness Randomized Clinical Trial," *Ophthalmology* (June 2016).

VEGF receptors are grafted onto an antibody "Fc" domain), EYLEA is likely to bind the VEGF target more tightly than LUCENTIS (which has only one VEGF binding domain), resulting in a stronger inhibition of VEGF in the patients' eyes. Furthermore, unlike LUCENTIS, which binds only to VEGF-A, EYLEA has the unique ability to bind to multiple VEGF family members, including VEGF-A, VEGF-B, and PIGF (placental growth factor). The three-dimensional configuration of EYLEA enables it to simultaneously bind both sides of the VEGF molecule in a "two-fisted grasp."

53. After years of research and development, and thorough regulatory review, EYLEA first received FDA approval in vial form in November 2011.[19] FDA designated EYLEA as a "Priority Review," which FDA only gives to drugs that represent "significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions when compared to standard applications."[20]

54. Following EYLEA's FDA approval, a clinical ophthalmologist and retina specialist at the Ophthalmic Consultants of Boston explained the benefits compared to LUCENTIS: "EYLEA offers the potential of achieving the efficacy we've come to expect from current anti-VEGF agents, ***but with less frequent injections and monitoring***. This may reduce the need for costly and time-consuming monthly visits for patients and caregivers."[21]

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[19] Press Release, Regeneron, "Regeneron Announces FDA Approval of EYLEA™ (aflibercept) Injection for the Treatment of Wet Age-Related Macular Degeneration," (Nov. 18, 2011), *available at* https://investor.regeneron.com/news-releases/news-release-details/regeneron-announces-fda-approval-eylea153-aflibercept-injection.

[20] U.S. Food and Drug Administration, "Priority Review," *available at* https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/priority-review (last visited July 13, 2020).

[21] Press Release, Regeneron, "Regeneron Announces FDA Approval of EYLEA™ (aflibercept) Injection for the Treatment of Wet Age-Related Macular Degeneration," (Nov. 18, 2011), *available at* https://investor.regeneron.com/news-releases/news-release-details/regeneron-announces-fda-approval-

55. Regeneron markets EYLEA in the United States while Bayer Healthcare ("**Bayer**") has the exclusive marketing rights for EYLEA outside the United States.

56. Since EYLEA's launch in vial form in 2011, Regeneron has not implemented any price increases in the U.S. market. This is unique when the average price of branded prescription drugs has increased by double-digit percentages annually.[22]

57. FDA approved EYLEA in a PFS form on August 13, 2019.[23] Regeneron started selling EYLEA PFS on December 9, 2019, and commenced a full-scale commercial launch in late February 2020. After only months on the market, physicians and patients have demonstrated an overwhelming preference for EYLEA PFS compared to the vial, and now ***approximately 80%*** of EYLEA sales are in PFS form. It is likely that nearly all EYLEA sales will convert to PFS within the year.

58. In addition, market share has already shifted from LUCENTIS PFS to EYLEA PFS within mere months of Regeneron's full-scale launch.

iii. BEOVU

59. BEOVU is the brand name for another anti-VEGF (brolucizumab-dbll) developed by Novartis. The FDA approved BEOVU in vial form for the treatment of wet AMD only on October 7, 2019, and Novartis launched BEOVU in the United States shortly thereafter.[24]

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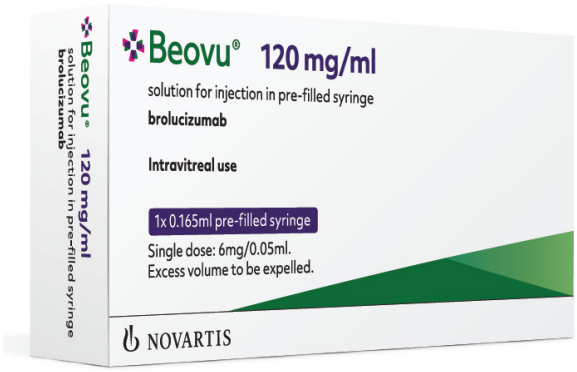
eylea153-aflibercept-injection.

[22] Producer Price Index by Industry: Pharmaceutical and Medicine Manufacturing, *available at* https://fred.stlouisfed.org/series/PCU32543254.

[23] Press Release, Regeneron, "FDA Approves EYLEA (aflibercept) Injection Prefilled Syringe," (Aug. 13, 2019), *available at* https://newsroom.regeneron.com/news-releases/news-release-details/fda-approves-eylear-aflibercept-injection-prefilled-syringe.

[24] Press Release, Novartis, "Novartis receives FDA approval for Beovu®, offering wet AMD patients vision gains and greater fluid reception vs aflibercept" (Oct. 8, 2019), *available at* https://www.novartis.com/news/media-releases/novartis-receives-fda-approval-beovu-offering-wet-amd-

60. Recognizing the overwhelming demand for anti-VEGFs in PFS form, Novartis is conducting clinical trials for a PFS version of BEOVU for the treatment of wet AMD in the United States. Upon information and belief, Novartis intends to seek FDA approval for, and launch, a PFS version of BEOVU.[25] According to Novartis, it "has [] engaged in significant work to prepare for offering a PFS presentation for BEOVU in the United States upon FDA approval, and has an anticipated timeline for FDA approval of the BEOVU PFS and subsequent launch in the United States."[26] Indeed, Novartis's October 8, 2019, press release announcing BEOVU's FDA approval featured an image of BEOVU in PFS form.[27]



61. Within mere months of BEOVU's launch, however, BEOVU patients experienced a range of severe safety issues. Physicians immediately began reporting that BEOVU patients were suffering from serious adverse reactions, including higher rates of intraocular inflammation ("**IOI**"), incidences of retinal artery occlusion ("**RAO**"), and occlusive retinal vasculitis ("**ORV**").

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patients-vision-gains-and-greater-fluid-reductions-vs-aflibercept.

[25] *See* ITC Compl. ¶ 6 ("Novartis is currently seeking FDA approval for BEOVU in a PFS presentation[.]"); *see also id.* at ¶ 69 ("Once FDA approval for the PFS presentation is achieved, Novartis has tangible plans to introduce the PFS to the market.").

[26] *See* ITC Compl. ¶ 24.

[27] Press Release, Novartis, "Novartis receives FDA approval for Beovu®," (Oct. 8, 2019), *available at* https://novartis.gcs-web.com/static-files/f3950fa0-a54d-4533-be36-4eed3baadc13.

62. IOI occurs when fluids or structures within the eye become inflamed from irritation or inflammation. IOI may result from use of a specific product that causes irritation, or it may result from an irritant or infectious agent brought into contact with the eye. IOI is an urgent medical condition that ranges in severity, and serious IOI can lead to blindness. RAO occurs when the retinal artery becomes blocked (occluded), and oxygen cannot be delivered to the eye. Depending on the location and severity of the blockage, RAO can rapidly lead to permanent blindness. ORV occurs when the inflammation in the eye (*i.e.*, IOI) is so severe that it narrows the retinal artery until it closes off (*i.e.*, an RAO), blocking blood flow to the retina. ORV can quickly result in irreversible blindness as blockage of the retinal artery means oxygen cannot be delivered to the retina. ORV is a new adverse event not seen in patients treated with EYLEA or other anti-VEGFs.

63. These incidences of IOI, RAO, and ORV prompted a prominent ophthalmology organization, the American Society of Retinal Specialists ("**ASRS**"), to issue ***five public warnings*** about the potential harmful effects of BEOVU. The ASRS released Safety Bulletins on January 22, February 23, March 30, April 7, and most recently on June 4, 2020, advising physicians about incidences of severe inflammation in patients injected with BEOVU. According to ASRS's February 23, 2020 announcement, "In addition to cases of mild-moderate intraocular inflammation [IOI], these reports have included 14 cases of vasculitis, of which 11 were designated as occlusive retinal vasculitis [ORV] by the reporting provider."[28] In response to physician and patient outcry, Novartis conducted an external safety review of BEOVU, examining post-marketing events in patients compared to its clinical trials.[29]

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[28] American Society of Retinal Specialists, "Beovu Update for ASRS Members," (Feb. 23, 2020), *available at* https://www.asrs.org/clinical/clinical-updates.

[29] Press Release, Novartis, "Novartis Completes Safety Review and Initiates Update to the Beovu® Prescribing Information Worldwide" (Apr. 8, 2020), *available at* https://www.novartis.com/news/novartis-

64. Given the severity of these adverse reactions suffered by BEOVU patients, Novartis ultimately sought FDA approval of an updated label for BEOVU to warn patients and physicians about the additional safety risks associated with the treatment. On June 11, 2020, Novartis received FDA approval for its new BEOVU label, which included an explicit "sub-section dedicated to retinal vasculitis and/or retinal vascular occlusion under 'Warnings and Precautions.'"[30] Novartis was forced to acknowledge that BEOVU may cause adverse events in patients of "retinal vasculitis and/or retinal vascular occlusion that may result in ***severe vision loss***. Typically these events occur in the presence of intraocular inflammation."[31]

iv. Other Anti-VEGF Drugs

65. Roche's Avastin® is the brand name for the anti-VEGF bevacizumab, which is a tumor-starving agent that is administered by slow injection into a patient's vein. Avastin is only FDA-approved for intravenous use for the treatment of certain cancers, including colon cancer, lung cancer, breast cancer, glioblastoma, and renal-cell carcinoma.[32] While some ophthalmologists use Avastin off-label due to its low-cost, Avastin is ***not FDA-approved*** to treat ophthalmic diseases and is only supplied by Roche/Genentech in vial form. Upon information and belief,

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completes-safety-review-and-initiates-update-beovu-prescribing-information-worldwide.

[30] Press Release, Novartis, "U.S. FDA Approves Updated Novartis Beovu® Label. To Include Additional Safety Information" (June 11, 2020), *available at* https://www.novartis.com/news/media-releases/us-fda-approves-updated-novartis-beovu-label-include-additional-safety-information#:~:text=Basel%2C%20June%2011%2C%202020%20%E2%80%94,and%20retinal%20vascular%20occlusion1.

[31] Press Release, Novartis, "Novartis Completes Safety Review and Initiates Update to the Beovu® Prescribing Information Worldwide" (Apr. 8, 2020) (emphasis added), *available at* https://www.novartis.com/news/novartis-completes-safety-review-and-initiates-update-beovu-prescribing-information-worldwide.

[32] U.S. Food and Drug Administration, Avastin® (bevacizumab), "Highlights of Prescribing Information, *available at* https://www.accessdata.fda.gov/drugsatfda_docs/label/2011/125085s225lbl.pdf.

Roche/Genentech does not plan to seek FDA approval for Avastin for the treatment of ophthalmic diseases.

66. Since Avastin is FDA-approved only as a cancer agent—and not as an ophthalmic treatment—Avastin is sold in large vials that are used to prepare an infusion. Unlike LUCENTIS, and EYLEA, Avastin is not offered in single-dose, ready-made vials or PFS appropriate for the treatment of ophthalmic diseases. Instead, before Avastin can be used to treat ophthalmic diseases, it must be "repackaged" by a third party pharmacy—*i.e.*, the repackaging pharmacy must remix or prepare a single dose of Avastin for eye injection from the larger treatment package that was intended for intravenous use in cancer patients. This repackaging process has raised concerns among physicians regarding sterility and dosing accuracy for Avastin. For example, as explained by a leading specialist in the ophthalmology field:

> Our evaluation showed significant differences in doses of compounded Avastin, as well as lower drug levels overall compared to Avastin that came from the manufacturer. This is troubling because the prescribed dosing regimen potentially won't produce the desired therapeutic response, or may put a patient's health at risk.[33]

67. Due to the potential health risks, a significant number of ophthalmologists and retinal specialists are unwilling to administer Avastin to their patients because they do not want to take the risk of off-label prescription as well as any potential errors that may have occurred during the third party repackaging process. Moreover, Avastin has shown to be less effective than EYLEA and LUCENTIS for the treatment of patients with certain ophthalmic diseases.[34]

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[33] "Study Shows Inconsistent Dosages of Widely Used Eye Disease Drug: Findings Add to Public Health Debate About Pharmacy Compounding," Weil Cornell Medicine (Sept. 18, 2014), *available at* https://news.weill.cornell.edu/news/2014/09/study-shows-inconsistent-dosages-of-widely-used-eye-disease-drug-szilard-kiss-donald-damico.

[34] *See* "Aflibercept, Bevacizumab, or Ranibizumab for Diabetic Macular Edema: Two-year Results from a Comparative Effectiveness Randomized Clinical Trial," *Ophthalmology* (June 2016).

68. Nevertheless, despite potential risks and the inconvenience of using Avastin, some physicians still choose to administer Avastin off-label because it is significantly cheaper than the anti-VEGFs for ophthalmic diseases. Avastin is much less expensive than LUCENTIS, BEOVU, or EYLEA because it is priced and dosed for the cancer treatment for which it is indicated. The large cancer-appropriate dose of Avastin, when repackaged into small ophthalmic doses, costs significantly less than anti-VEGFs indicated for ophthalmic diseases.

69. Notably, Avastin is also manufactured and sold by Roche. Given that Novartis owns a 33.3% stake in Roche, any profits from off-label usage of Avastin still flow to Novartis due to its substantial ownership interest in Roche.

70. Macugen (pegaptanib sodium injection) was the first anti-VEGF approved by the FDA in 2004 to treat wet AMD. While still technically available, newer anti-VEGFs, including EYLEA and LUCENTIS, have shown to be more effective than Macugen. As a result, Macugen is rarely prescribed or used for the treatment of wet AMD anymore.

D. PFS Are the Preferred Format for Anti-VEGF Treatments

71. In order to administer anti-VEGFs supplied in vials to patients, the ophthalmologist or retinal specialist must perform a sterile, multi-step process at the time of administration. As illustrated below, EYLEA in vial form comes with multiple components, including the vialed biologic, two separate needles, and a plastic syringe.[35] To administer, the ophthalmologist must first use the filter needle to withdraw the correct amount of the anti-VEGF from the vial and then switch to an injection needle before injecting the properly measured dosage into the patient's eye—all under sterile conditions.

[35] *See* "EYLEA Biologics License Application FDA Approval Letter" Department of Health and Human Services (November 18, 2011), *available at* https://hcp.eylea.us/mediadb/fda-approval-letter-wet-amd.pdf.

72. By contrast, an anti-VEGF PFS—like EYLEA PFS pictured below[36]—is a single, integrated safety system injection product that comes ready-to-use as soon as the ophthalmologist opens the box and attaches a needle for injection.

73. Thus, administering EYLEA in vial form, by definition, has more touch points, is more time-consuming, increases the number of steps and thereby the possibility of foreign particles being introduced into the eye during administration. There has therefore been a general trend in the pharmaceutical industry away from vials towards prefilled syringes due to multiple advantages and the overwhelming preference of ophthalmologists. As explained in an article in *Retinal Physician*, "Chronic, serial intravitreal injections are most efficiently performed with prefilled

[36] *See* Regeneron, "About Eylea," *available at* https://hcp.eylea.us (last visited July 12, 2020).

syringes."[37] Anti-VEGF PFS "are a boon to patients requiring this treatment . . . and retinal physicians because of the decreased endophthalmitis risk, dose accuracy, and improved clinic efficiency they can provide."[38]

74. First, administering the anti-VEGF in a PFS enables the required dose to be delivered more precisely. As a result, only trace amounts of the anti-VEGF remain in the PFS after injection. In contrast, vials require physicians to overfill the drug to ensure that an accurate dose is pulled into the syringe each time. One "recent 'real world' study evaluated the accuracy and precision of anti-VEGF volume delivery in the real-world setting [and] demonstrated that the use of a prefilled syringe was associated with improved anti-VEGF dosing accuracy."[39]

75. PFS also can enhance patient quality of life and reduce patient time in the clinic. This is especially important in today's climate where the vulnerable elderly population—representing the majority of patients receiving anti-VEGF treatments—is already at an increased risk for the COVID-19 pandemic. PFS are also more efficient for the administering physician, and in one study, use of PFS demonstrated a 40% reduction in office preparation time compared to vials.[40] PFS save time and effort for the physician, which quickly adds up in busy ophthalmologist practices. This also allows the administering physician to treat more patients.

76. PFS also reduce the possibility of foreign particles being introduced into the eye during administration. Repeated intravitreal injections necessarily pose some risk of

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[37] Michael Colucciello, M.D., "Prefilled Syringe Delivery of Intravitreal Anti-VEGF Medications: Advantages for Patients and Physicians," *Retinal Physician* (Mar. 1, 2019), *available at* https://www.retinalphysician.com/issues/2019/march-2019/prefilled-syringe-delivery-of-intravitreal-anti-ve#reference-15.

[38] *Id.*

[39] *Id.*

[40] *Id.*

endophthalmitis for patients. Endophthalmitis is an inflammation of the interior of the eye that can cause serious complications. PFS help to minimize this risk by reducing the number of steps and touch points prior to administration.[41]

77. As summarized by Novartis:

> The injection itself carries a risk of complications including infection, inflammation, introduction of particles in the eye, and even blindness. To address the problems associated with injection of VEGF-antagonists into the eye . . . pre-filled, sterilized syringes . . . permit more safe, effective and efficient injections of VEGF-antagonists into the eye.[42]

78. Novartis/Genentech and Regeneron therefore sought to develop and launch PFS versions of their respective anti-VEGFs for the treatment of certain ophthalmic diseases.

79. Following Novartis's license to Genentech for the '631 Patent, Novartis/Genentech developed and obtained FDA approval for LUCENTIS in PFS form in October 2016 and launched it in the United States in early 2017. As explained in the accompanying press release, "The LUCENTIS PFS allows physicians to eliminate several steps in the preparation and administration process, including disinfecting the vial, attaching a filter needle, drawing the medicine from the vial using the needle, removing the filter needle from the syringe and replacing with an injection needle."[43] PFS thus provide significant benefits in terms of convenience and ease of use compared to vials. Indeed, a 2018 study funded by Genentech and conducted on the usability of LUCENTIS found that medical professionals were able to successfully administer the treatment with 91% reporting that they found the LUCENTIS PFS "easy" or "very easy" to use.[44]

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41 *Id.*

42 Compl. at 1., *Novartis Pharma AG et al. v. Regeneron Pharm. Inc.*, No. 1:20-cv-00690 (N.D.N.Y. June 19, 2020) (the "Novartis NDNY Compl.").

43 Press Release, Genentech, "FDA Approves Genentech's Lucentis® (Ranibizumab Injection) Prefilled Syringe," (Oct. 14, 2016), *available at* https://www.gene.com/media/press-releases/14640/2016-10-14/fda-approves-genentechs-lucentis-ranibiz.

44 Andrew N. Antoszyk, Carl Baker, Jorge Calzada, et al., *Usability of the Ranibizumab 0.5 mg*

80. Following the U.S. launch of LUCENTIS PFS in 2017, there was a "strong uptake" with a "more than 80% conversion rate" from LUCENTIS vials to PFS.[45] In fact, Genentech experienced severe supply shortages following the launch of LUCENTIS PFS due to an increase in demand for PFS. In early 2018, "LUCENTIS grew at 6% for the quarter driven by volume due to [the] successful launch of the first prefilled syringe" to treat ophthalmic diseases.[46] Roche touted "increasing market shares in all approved indications" due to LUCENTIS PFS' "competitive advantage,"[47] stating that it "underestimated the competitive dynamics of the prefilled syringe."[48] Novartis has similarly recognized that "LUCENTIS' 18% U.S.-based sales 'growth was driven by sales of prefilled syringes and sales increases in all approved indications.'"[49] Nearly all LUCENTIS sales today are in PFS rather than vial form.

81. Until the recent launch of EYLEA PFS in the United States, LUCENTIS PFS was effectively the only FDA-approved anti-VEGF for the treatment of certain ophthalmic diseases available for sale in a PFS.[50] LUCENTIS PFS possessed virtually 100% share of the anti-VEGF PFS market from the time of its 2017 launch until EYLEA PFS was introduced in late 2019. As

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Prefilled Syringe: Human Factors Studies to Evaluate Critical Task Completion by Healthcare Professionals, PDA Journal of Pharmaceutical Science and Technology, 72(4) 411-419 (July 2018), *available at* https://journal.pda.org/content/72/4/411.

[45] Roche, 1st Quarter Conference Call (Apr. 27, 2017), *available at* https://www.roche.com/investors/agenda/q1-2017.htm.

[46] Roche, First Quarter Sales 2018 Audio Webcast Replay, (Apr. 26, 2018), *available at* https://www.roche.com/investors/agenda/q1-2018.htm.

[47] *Id.*

[48] *Id.*

[49] ITC Compl. ¶ 73.

[50] While Macugen received FDA approval in 2004 for a prefilled syringe to treat wet AMD only, it is also an older, less effective treatment that is rarely prescribed anymore, if at all.

for Novartis's other anti-VEGF treatment, BEOVU, it is not yet available in the United States in PFS.

82. Regeneron received FDA approval in August 2019 for EYLEA PFS and began selling it in December 2019 with a full-scale commercial launch in late February 2020. As explained in Regeneron's press release, "[t]he sterilized prefilled syringe offers the same medicine as the currently available EYLEA, in an ***easier to use and administer presentation***."[51] The PFS "provides physicians with a new way to administer EYLEA that requires fewer preparation steps compared to vials."[52] That is why the uptake of EYLEA PFS was similar to what happened when LUCENTIS PFS launched. Within mere months of Regeneron's commercial launch, approximately 80% of all EYLEA sales are now in PFS.

83. Given the benefits to both physicians and patients for PFS, anti-VEGF PFS have become the standard treatment for ophthalmic diseases. Physicians have reported that the availability of PFS is a key driver of competition among anti-VEGFs. Indeed, market data show that once a PFS launches, physicians rapidly converted their patients from the vial version to the PFS version at a rate of approximately 80% to 90%. The importance of this delivery method is further supported by how some sales of the vial form of EYLEA—particularly for new patients—were being captured by LUCENTIS PFS sales despite EYLEA being regarded by many physicians and patients as the superior product.

84. Recognizing that the playing field for competition among FDA-approved anti-VEGFs for ophthalmic diseases has changed over from vials to PFS, Novartis and Vetter have

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[51] Press Release, Regeneron, "FDA Approves EYLEA (aflibercept) Injection Prefilled Syringe," (Aug. 13, 2019) (emphasis added), *available at* https://newsroom.regeneron.com/news-releases/news-release-details/fda-approves-eylear-aflibercept-injection-prefilled-syringe.

[52] *Id.*

engaged in the anticompetitive behavior described herein to unreasonably restrain competition for—and the availability of—anti-VEGF PFS treatments.

E. Novartis's History of Anticompetitive Behavior with LUCENTIS

85. Novartis has already demonstrated a propensity to engage in anticompetitive conduct to insulate LUCENTIS from competition. In 2012, Novartis and Roche engaged in an anticompetitive scheme in Europe related to LUCENTIS, resulting in a €183 million fine (or approximately $210 million USD) imposed by European antitrust regulators.[53]

86. In 2014, the Italian Competition Authority determined that Novartis and Roche had unlawfully conspired to increase the use of LUCENTIS by discouraging the off-label use of a cancer drug that was approximately 40 times cheaper.[54] Internal Novartis documents demonstrated that Novartis had purposely sought to "leverage safety data and regulator" statements to discourage off-label drug use to prevent the erosion of LUCENTIS sales.[55] The Italian Competition Authority concluded that the two companies improperly cast doubt on the safety of the cheaper, off-label drug, exaggerating its side effects in order to shift demand to the much more expensive LUCENTIS.[56] As the Italian authorities explained, Novartis benefitted from the increased direct

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[53] Press Release, European Commission, "Italy: The Italian Competition Authority Fines Roche and Novartis for Cartelizing Sales of Two Major Ophthalmic Medicines," (Feb. 27, 2014), *available at* http://ec.europa.eu/competition/ecn/brief/02_2014/it_roche.pdf.

[54] *See* Novartis, 2018 Annual Report, *available at* https://www.novartis.com/sites/www.novartis.com/files/novartis-annual-report-2018-en.pdf.

[55] European Commission, Report from the Commission to the Council and the European Parliament, *Competition Enforcement in the Pharmaceutical Sector (2009–2017)* (Jan. 28, 2019), *available at* https://data.consilium.europa.eu/doc/document/ST-6232-2019-INIT/en/pdf. Novartis also publicly declared that the Italian Competition Authority's decision "openly encourage[d] and promote[d] the widespread unlicensed intravitreal use of Avastin contrary to the requirements of European and Italian regulatory law" and "undermine[d] the European regulatory framework designed to protect patient safety." David Jolly, *Italy Fines Novartis and Roche in Collusion Case*, N.Y. Times, Mar. 5, 2014, *available at* https://nyti.ms/1ibZVoT.

[56] Press Release, European Commission, "Italy: The Italian Competition Authority Fines Roche and

sales of LUCENTIS in Europe while Roche benefitted indirectly through royalties received by Genentech through its licensing agreement with Novartis. This misleading and anticompetitive conduct resulted in ***$60 million in additional costs*** to the Italian National Health Service in 2012.

87. Novartis and Roche challenged the Italian regulators' 2014 judgment in an appeal to the Court of Justice of the European Union. Novartis argued that its agreement with Roche simply amounted to an exclusive licensing arrangement. The European authorities rejected this claim: "The arrangement was not designed to restrict the commercial autonomy of the parties to the licensing agreement regarding LUCENTIS but rather the conduct of third parties – in particular healthcare professionals – with a view to reducing the prescription of [the off-label drug product] in ophthalmology for the benefit of LUCENTIS. In those circumstances, the arrangement cannot be considered to be ancillary and objectively necessary for the implementation of the licensing agreement."[57] In 2018, the European authorities upheld the Italian Competition Authority's findings and €183 million fine (approximately $210 million USD).

88. Novartis's pattern of abusive and anticompetitive conduct also has attracted the attention of other competition regulators. In 2012, the French Competition Authority initiated an investigation into anticompetitive practices in the anti-VEGF market for the treatment of wet AMD. In 2019, the French Competition Authority initiated formal charges by issuing a Statement of Objections against Novartis alleging anticompetitive practices similar to those alleged by the Italian Competition Authority. In these formal antitrust charges, the French Competition Authority

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Novartis for Cartelizing Sales of Two Major Ophthalmic Medicines," (Feb. 27, 2014), *available at* http://ec.europa.eu/competition/ecn/brief/02_2014/it_roche.pdf.

[57] Press Release No 06/18, Court of Justice of the European Union, "The agreement between the pharmaceutical groups Roche and Novartis designed to reduce the use of Avastin in ophthalmology and to increase the use of Lucentis might constitute a restriction of competition 'by object'" (Jan. 23, 2018), *available at* https://curia.europa.eu/jcms/upload/docs/application/pdf/2018-01/cp180006en.pdf.

alleged that Novartis and Roche engaged in anticompetitive conduct in the French market for anti-VEGFs for the treatment of wet AMD from 2008 to 2013.[58]

89. Novartis's history of collusion is illustrative of its intent to insulate LUCENTIS (and now LUCENTIS PFS) from competition globally, including in the United States. Similar to the Novartis/Roche scheme in Europe, Novartis's anticompetitive conduct in the United States has been designed to prevent Regeneron from launching—and now selling—EYLEA PFS in order to steer physicians and patients away from alternative anti-VEGF ophthalmic treatments, regardless of the benefits of those treatments.

F. Novartis's Fraud on the USPTO to Obtain the '631 Patent

90. At the heart of Defendants' anticompetitive conduct is the '631 Patent that Novartis procured through fraud on the USPTO. The '631 Patent issued on December 29, 2015, and it was assigned to Novartis AG. In February 2020, ownership of the '631 Patent was transferred to Novartis Technology LLC, Novartis Pharmaceuticals Corporation, and Novartis Pharma AG, the three Novartis Defendants. The '631 Patent term extends until 2033.

91. Independent claim 1 of the '631 Patent is reproduced below.

[58] *See* Novartis, 2018 Annual Report at F-50 – F-51, *available at* https://www.novartis.com/sites/www.novartis.com/files/novartis-annual-report-2018-en.pdf.

> **1**. A pre-filled, terminally sterilized syringe for intravitreal injection, the syringe comprising a glass body forming a barrel, a stopper and a plunger and containing an ophthalmic solution which comprises a VEGF-antagonist, wherein:
>
> (a) the syringe has a nominal maximum fill volume of between about 0.5 ml and about 1 ml,
>
> (b) the syringe barrel comprises from about 1 µg to 100 ug silicone oil,
>
> (c) the VEGF antagonist solution comprises no more than 2 particles >50 µm in diameter per ml and wherein the syringe has a stopper break loose force of less than about 11N.

'631 Patent, Claim 1

92. The '631 Patent is unenforceable due to the inequitable conduct of at least Individual #1,[59] a Novartis employee and the lead inventor of the '631 Patent, and at least Individual #2 and Individual #3, who were the primary patent practitioners at Novartis responsible for the prosecution of the application that led to the issuance of the '631 Patent. Individuals #1, #2, and #3, who were all subject to a continuing duty to disclose information material to patentability, deliberately withheld prior art disclosing terminal sterilization of a prefilled syringe containing a VEGF antagonist, which the individuals knew was material to the patentability of claims of the '631 Patent. As detailed below, the claims of the '631 Patent would not have been allowed had the examiner conducting the examination of application for the '631 Patent been aware of the undisclosed prior art. At least Individuals #1, #2, and #3 knew of the materiality of

[59] We are aware of *Signify N. Am. Corp. v. Reggiani Lighting USA, Inc.*, No. 18-CIV-11098, 2020 WL 1331919 (S.D.N.Y. Mar. 23, 2020), in which a complaint was dismissed for failure to identify the individuals involved in an inequitable conduct allegation with specificity. However, Regeneron believes that Novartis is fully aware of the identity of Individuals #1, #2, and #3, and Regeneron chose not to publicly disclose their names as a matter of professional courtesy. If Novartis intends to seek dismissal of the complaint based on the failure to identify these individuals with specificity, or if the Court has a question about the sufficiency of the pleading for this reason, Regeneron respectfully requests the opportunity to amend its complaint to identify the individuals by name.

this prior art based on office actions by a different set of examiners during prosecution of a parallel patent family, but deliberately withheld the information demonstrating unpatentability from the examiner that was conducting the examination of the application for the '631 Patent. The single most reasonable inference that may be drawn from the evidence described below is that the Individuals #1, #2, and #3 withheld this material prior art with an intent to deceive the USPTO.

93. Because patents affect the public interest and patent examinations are conducted *ex parte*, the USPTO and courts impose a duty of candor and disclosure upon inventors (such as Individual #1), patent applicants, and their representatives before the USPTO (e.g., registered patent attorneys and agents such as Individuals #2 and #3). As part of this duty, the USPTO requires inventors, patent applicants and their representatives to disclose to the examiner—through the Information Disclosure Statement ("**IDS**")—all "information known to that individual to be material to patentability." *See* 37 C.F.R. § 1.56. This duty of candor includes the duty to supplement the IDS with any material information or references the inventors, applicants or their representatives become aware of after the initial filing of the patent application up to and including the date of issuance of the patent.

i. The Prosecution of U.S. Patent Application No. 13/750,352 That Ultimately Issued as the '631 Patent

94. The application for the '631 Patent (App. No. 13/750,352) ("the '352 Application") was filed on January 25, 2013. The application data sheet was signed by Individual #2, and Individual #1 also submitted an inventor declaration pursuant to 37 C.F.R. § 1.63. The '352 Application included one independent claim and thirty-one dependent claims directed to a prefilled syringe, blister packs comprising a prefilled syringe and a method of treating a patient using the prefilled syringe. As shown below, originally filed claim 1 was directed to structural aspects of the prefilled syringe, the fill volume of the syringe, the dosage volume of the VEGF antagonist

solution, the amount of silicone oil on the syringe barrel, and the number of particles in the VEGF antagonist solution.

> 1. A pre-filled syringe, the syringe comprising a glass body, a stopper and a plunger, the body comprising an outlet at an outlet end and the stopper being arranged within the body such that a front surface of the stopper and the body define a variable volume chamber from which a fluid can be expelled though the outlet, the plunger comprising a plunger contact surface at a first end and a rod extending between the plunger contact surface and a rear portion, the plunger contact surface arranged to contact the stopper, such that the plunger can be used to force the stopper towards the outlet end of the body, reducing the volume of the variable volume chamber, characterised in that the fluid is an ophthalmic solution which comprises a VEGF-antagonist wherein:
>
> (a) the syringe has a nominal maximum fill volume of between about 0.5ml and about 1ml,
>
> (b) the syringe is filled a dosage volume of between about 0.03ml and about 0.05ml of said VEGF antagonist solution,
>
> (c) the syringe barrel comprises less than about 500µg silicone oil, and
>
> (d) the VEGF antagonist solution comprises no more than 2 particles ≥50µm in diameter per ml.

'352 Application, Originally Filed Claim 1

95. In a preliminary amendment on August 16, 2013, before any office actions had been received from the USPTO, claim 1 was amended by deleting most of the structural limitations for the syringe as shown below (deleted material is stricken and newly added material is underlined). The preliminary amendment was signed by Individual #2.

1.(currently amended) A pre-filled syringe for intravitreal injection, the syringe comprising a glass body forming a barrel, a stopper and a plunger, ~~the body comprising an outlet at an outlet end and the stopper being arranged within the body such that a front surface of the stopper and the body define a variable volume chamber from which a fluid can be expelled though the outlet, the plunger comprising a plunger contact surface at a first end and a rod extending between the plunger contact surface and a rear portion, the plunger contact surface arranged to contact the stopper, such that the plunger can be used to force the stopper towards the outlet end of the body, reducing the volume of the variable volume chamber, characterised in that the fluid is an~~ and containing an ophthalmic solution which comprises a VEGF-antagonist, wherein:

(a) the syringe has a nominal maximum fill volume of between about 0.5ml and about 1ml,

(b) the syringe is filled with a dosage volume of between about 0.03ml and about 0.05ml of said VEGF antagonist solution,

(c) the syringe barrel comprises less than about 500µg silicone oil, and

(d) the VEGF antagonist solution comprises no more than 2 particles ≥50µm in diameter per ml.

'352 Application, First Amendment to Claim 1

96. The '352 Application was examined by USPTO examiner Aarti Bhatia Berdichevsky (the "**Syringe Examiner**"). In a first office action on May 14, 2014, the Syringe Examiner issued a non-final rejection determining that claim 1 was both anticipated and obvious in view of a published patent application identified as WO 2007/035621 to Scypinski. In addition, the Syringe Examiner determined that all of the other pending claims (2-32) were either anticipated by Scypinski, or obvious in view of Scypinski alone of in view of a second published patent application, US 2011/0276005 to Hioki.

97. On August 13, 2014, the Novartis applicant submitted a response to the non-final rejection. The response included an amendment to claim 1, as shown below, that amended the claimed range of silicone oil from "less than about 500 µg" to "from about 1 µg to 500 µg." No other changes were made to claim 1. Claims 7, 8, and 11 were cancelled and dependent claims 33 and 34 were added. The response argued that the claims were not anticipated or obvious, specifically focusing on the silicone oil limitation and arguing that "the applicants have

surprisingly found that using less silicone actually leads to usable syringes." The response was signed by Individual #3.

> 1.(Currently amended) A pre-filled syringe for intravitreal injection, the syringe comprising a glass body forming a barrel, a stopper and a plunger and containing an ophthalmic solution which comprises a VEGF-antagonist, wherein:
>
> (a) the syringe has a nominal maximum fill volume of between about 0.5ml and about 1ml,
>
> (b) the syringe is filled with a dosage volume of between about 0.03ml and about 0.05ml of said VEGF antagonist solution,
>
> (c) the syringe barrel comprises ~~less than~~ from about 1µg to 500µg silicone oil, and
>
> (d) the VEGF antagonist solution comprises no more than 2 particles >50µm in diameter per ml.

'352 Application, Second Amendment to Claim 1

98. In a second office action dated August 26, 2014, the Syringe Examiner issued a final rejection of all pending claims. The Syringe Examiner determined that the claims as amended were obvious in view of the same prior art (Scypinski and Hioki), finding that "[i]t would have been within the level of ordinary skill in the art to find the optimum value of silicone oil to use, and to find the optimum amount to achieve the desired slide force and break loose force." 8/26/14 Office Action at 5.

99. On November 24, 2014, the Novartis applicant responded to the final office action and requested continued examination. Claim 1 was amended again, as shown below, by deleting the dosage volume limitation, narrowing the limitation for the amount of silicone oil from "1 µg to 500 µg" to "1 µg to 100 µg," and adding a limitation for the stopper break loose force. The response again argued that "the applicants have surprisingly found that using less silicone actually leads to usable syringes." The response was signed by Individual #3.

1.(Currently amended) A pre-filled syringe for intravitreal injection, the syringe comprising a glass body forming a barrel, a stopper and a plunger and containing an ophthalmic solution which comprises a VEGF-antagonist, wherein:

(a) the syringe has a nominal maximum fill volume of between about 0.5ml and about 1ml,

~~(b) the syringe is filled with a dosage volume of between about 0.03ml and about 0.05ml of said VEGF antagonist solution,~~

(b) ~~(c)~~ the syringe barrel comprises from about 1µg to 100ug ~~500µg~~ silicone oil, ~~and~~

(c) ~~(d)~~ the VEGF antagonist solution comprises no more than 2 particles >50µm in diameter per ml and

wherein the syringe has a stopper break loose force of less than about 11N.

'352 Application, Third Amendment to Claim 1

100. On December 12, 2014, in a third office action, the Syringe Examiner issued a non-final rejection of all pending claims. The Syringe Examiner maintained that the claims were obvious based on Scypinski in view of Hioki. The Syringe Examiner also rejected the argument put forward by Individual #3 and the Novartis applicant that they had "surprisingly" found that using less silicone actually leads to usable syringes. The Syringe Examiner stated that "it would be obvious to one having ordinary skill in the art to try and use less silicone, since it is common sense to use as little as possible to achieve the desired effect." 12/12/14 Office Action at 5.

101. The Novartis applicant submitted a response to the non-final rejection on March 11, 2015. The response again focused on the purported non-obviousness of the silicone oil limitation. Specifically, the response argued that "it has to be noticed that the cited prior art does not contain any suggestion whatsoever regarding silicone content of less than 500 µg in the glass cylinder of pre-filled syringes for ophthalmic use, as it is determined by the claims. The lack of any suggestion in order to reach this value shows that the current invention is not obvious in view of the documents cited by the Examiner." 3/11/15 Response at 7. The response also included commentary regarding terminal sterilization of syringes, noting that "the prefilled syringe is terminally sterilized as well, whereby the syringe is typically already located in its package" and

that "[i]f the pre-filled syringe is not appropriately sealed, significant amounts of [sterilizing] gas may intrude into the volume chamber of the syringe and have a detrimental effect on the drug." *Id.* at 5. The Novartis applicant made no amendments to the claims in the March 11, 2015 response, which was signed by Individual #3.

102. On March 20, 2015, in a fourth office action, the Syringe Examiner issued a final rejection as to all pending claims, maintaining the same rejections and arguments as those put forward in the December 12, 2014 office action. With respect to the discussion of terminal sterilization in the March 11, 2015 response, the Syringe Examiner explained that terminal sterilization was not claimed. Specifically, the Syringe Examiner stated that "it is noted that the features upon which applicant relies (i.e., the prefilled syringe is terminally sterilized) is not recited in the rejected claim(s)." The Syringe Examiner further expressed that the "prior art meets the claims as currently presented." 3/20/15 Office Action at 2-3.

103. On July 17, 2015, after the fourth office action, the Novartis applicant again requested continued examination and submitted a response amending claim 1. As shown below, the amendment to claim 1 added the limitation "terminally sterilized." The response stated that "independent claim 1 now recites that the prefilled syringe is terminally sterilized" and argued that "a prima facie case of obviousness has not been established." Thus, after more than two years of examination focused on the patentability of a syringe with low levels of silicone oil, the Novartis applicant shifted the focus of patentability to the question of whether terminally sterilized prefilled syringes were known or obvious in view of the prior art. The July 17, 2015 response was signed by Individual #4, another attorney at Novartis.

1.(Currently amended) A pre-filled, terminally sterilized syringe for intravitreal injection, the syringe comprising a glass body forming a barrel, a stopper and a plunger and containing an ophthalmic solution which comprises a VEGF-antagonist, wherein:

(a) the syringe has a nominal maximum fill volume of between about 0.5ml and about 1ml,

(b) the syringe barrel comprises from about 1µg to 100ug silicone oil,

(c) the VEGF antagonist solution comprises no more than 2 particles >50µm in diameter per ml and wherein the syringe has a stopper break loose force of less than about 11N.

'352 Application, Fourth Amendment to Claim 1

104. On August 19, 2015, the Syringe Examiner relented and issued a notice of allowance. First, the Syringe Examiner noted that on August 10, 2015, she conducted a telephone interview with Individual #3 and received authorization from him to make an "examiner's amendment" to one of the claims. Second, the Syringe Examiner stated as reasons for allowing the claims as amended to issue that "the ***prior art of record*** fails to disclose either singly or in combination the claimed device of a prefilled glass syringe…that is prefilled with a VEGF antagonist ***and is terminally sterilized as successfully amended and argued by the Applicant***" 8/19/15 Notice of Allowance at 2 (emphasis added).

105. As explained above, the examination by the Syringe Examiner to that point in time had been focused on the amount of silicone oil used on a syringe barrel, based on the arguments advanced by the Novartis applicant and their attorney Individual #3. The Syringe Examiner thus focused on prior art (Scypinski and Hioki) that demonstrated that those arguments were without merit. But the Novartis applicant and their attorneys then shifted their strategy and for the first time, after nearly 15 months of futile argument with the Syringe Examiner, introduced the issue of whether the prior art discloses terminal sterilization of a prefilled syringe. However, as detailed below, at least Individuals #1, #2, and #3 knew of prior art and other determinations by the USPTO regarding the obviousness of terminally sterilizing a prefilled syringe containing an anti-VEGF, and deliberately withheld with an intent to deceive that prior art and other determinations by the

USPTO regarding terminal sterilization from the Syringe Examiner. The Syringe Examiner would not have allowed the claims of the '631 Patent if the Syringe Examiner had been aware of the undisclosed prior art and the USPTO's other determinations regarding the obviousness of terminally sterilizing a prefilled syringe containing an anti-VEGF.

ii. The Overlapping Examination of U.S. Patent Application No. 13/382,380 Relating to Terminal Sterilization of a Prefilled Syringe

106. The examination of the application for the '631 Patent overlapped with the prosecution of another Novartis application—U.S. Patent Application No. 13/382,380 (the "**'380 Application**") that, as shown in the excerpts below, was directed to terminally sterilizing a prefilled syringe containing a biological drug product, and specifically, ranibizumab (the active ingredient in LUCENTIS), an anti-VEGF:

'380 Application, Specification at p. 1
"This invention relates to a method and system for terminal sterilization of the outer surface and/or surface decontamination of prefilled containers in secondary packaging, wherein the prefilled container contains a pharmaceutical or biological drug product."

'380 Application, Specification at p. 2
"Terminal sterilization of prefilled containers in secondary packaging is one way to provide the device to an end user with a low bio-burden and low risk of contaminants, for safe application of the product by the end user. Moreover, there is a strong market need for terminally antimicrobially-treated medical devices, such as prefilled syringes used for intravitreal injections."

'380 Application, Specification at p. 3
"Described herein is a terminal sterilization and surface decontamination treatment of prefilled containers, specifically for sterilization of prefilled containers containing sensitive solutions, such as a drug product or biologic therapeutic, within secondary packaging. In one embodiment, terminal sterilization is achieved by treating prefilled containers within secondary packaging with controllable vaporized-hydrogen peroxide (VHP)."

'380 Application, Specification at 9
"In one particular embodiment, the drug product is a protein solution, such as ranibizumab (e.g., 6 mg/ml or 10 mg/ml) solution for intravitreal injection."

107. Individual #1, the first named inventor of the '631 Patent, is the sole named inventor of the subject matter set forth in the '380 Application. Individuals #2 and #3, two practitioners who prosecuted the application that became the '631 Patent, were the very same practitioners prosecuting the '380 Application. The '380 Application is a U.S. application related to International Application No. PCT/EP2010/060011. Specifically, the '380 Application and International Application No. PCT/EP2010/060011 both claim priority to patent application 09165456.6 filed in the European Patent Office. The '380 Application and International Application No. PCT/EP2010/060011 contain materially identical disclosures. International Application No. PCT/EP2010/060011 was published as WO 2011/006877 ("WO '877") on January 20, 2011, which is one and a half years ***before*** the filing date of the earliest priority application of the '631 Patent. Accordingly, WO '877, which includes the same disclosure as the '380 Application of a terminally sterilized prefilled syringe containing an anti-VEGF, is prior art to the '631 Patent under pre-AIA 35 U.S.C. § 102(b) ("[T]he invention was patented or described in a printed publication in…a foreign country…more than one year prior to the date of the application for the patent in the United States.").

108. The '380 Application was filed on January 5, 2012 and the examination was conducted by ***different*** USPTO examiners (Donald Spamer, Gordon R. Baldwin and Sean E. Conley; collectively, the **"Sterilization Examiners**") than the application for the '631 Patent. The Sterilization Examiners were part of Art Unit 1775, which is directed to chemical compositions, whereas the Syringe Examiner was part of Art Unit 3763, which is directed to surgical devices. And unlike the examination of the application for the '631 Patent, the examination of the '380 Application was entirely focused on the issue of whether terminal sterilization of a prefilled syringe containing an anti-VEGF would have been obvious. As detailed below, over the course of

five office actions between January 2013 and April 2014, the Sterilization Examiners repeatedly and consistently found that terminal sterilization of a prefilled syringe for intravitreal injection containing an anti-VEGF was obvious in view of certain prior art.

109. In a first office action on September 14, 2012, the Sterilization Examiners issued a non-final rejection determining that the terminal sterilization subject matter being sought by the Novartis applicant in the '380 Application was anticipated by U.S. 2003/0003014 ("**Metzner**"), published on January 2, 2003, and obvious based on Metzner in view of U.S. 6,228,324 ("**Hasegawa**"), patented on May 8, 2001. The Sterilization Examiners made numerous findings to support the rejection, including that "Metzner et al. teaches a method for surface decontamination of a prefilled container in secondary packaging…the use of vaporized hydrogen peroxide in order to sterilize the surfaces of the packaging…that the hydrogen peroxide is left in contact with the surfaces for a sufficient amount of time to achieve decontamination…[and] also teaches the use of post-decontamination measures of applying a vacuum…[which] would remove the hydrogen peroxide as evidence by Hasegawa et al." 9/15/12 Office Action at 2-3. The Sterilization Examiners further found that "Metzner et al. teaches that this method can be done on temperature sensitive pharmaceutical products…that the protein drug product is in a carpule…[which] is a container for medicine that is administered to the patient with a syringe" and that "[a] person having ordinary skill in the art at the time of the invention would understand that if this method is capable of sterilizing prefilled protein drug products in secondary packaging without causing degradation of the proteins that the method is capable of treating the specific protein ranibizumab." *Id.* at 3.

110. The Novartis applicant submitted a response on December 12, 2012. The response included an amendment to the proposed independent claim, withdrew a number of claims, and

contested the Sterilization Examiners' determinations of anticipation and obviousness. The response was signed by Individual #2.

111. In a second office action on January 3, 2013, the Sterilization Examiners issued a final rejection. In this final rejection, the Sterilization Examiners maintained the obviousness of the terminal sterilization subject matter in view of Metzner and Hasegawa, further in view of U.S. Patent 5,788,941 to Dalmasso. For example, the Sterilization Examiners noted that "the combination of Metzner et al. and Hasegawa et al. teaches that the hydrogen peroxide vapor sterilization method can be used for sterilizing prefilled syringes in secondary packaging where the prefilled drug product is various proteins." 1/13/13 Office Action at 6.

112. The Novartis applicant submitted a response to the second office action on May 3, 2013 and requested continued examination. The Novartis applicant again contested the Sterilization Examiners determination of obviousness, this time submitting a declaration from Individual #1. In that declaration, Individual #1 stated that "the Examiner's conclusion with regard to Metzner is incorrect" and that "[t]he method taught by Metzner would likely result in denaturation of the protein in the syringe, or a non-sterile pre-filled syringe, or both." 5/3/13 Individual #1 Declaration at ¶ 7. Individual #1 further stated that "[t]he present application disclosed for the first time, and contrary to conventional thinking, that it is possible to obtain sufficient sterilization of the outer surface of a syringe in secondary packaging at ambient pressure." *Id.* at ¶ 9. The May 3, 2013 response was signed by Individual #2.

113. In a third office action on June 14, 2013, the Sterilization Examiners issued a non-final rejection. The Sterilization Examiners considered Individual #1's declaration and concluded that "the Affiant merely makes conjectures that the combination of Metzner and Hasegawa (using the method of Metzner to sterilize a drug filled syringe in secondary packaging) would be

deleterious through statements such as 'would likely result in denaturation' and 'may not result in a sterile product.' The Affiant has not provided any factual evidence or proof of these conjectures." 6/14/13 Office Action at 2. The Sterilization Examiners found that "Metzner does in fact recognize these possibilities and teaches that if movement of a plunger or leaking seel [*sic*] is a concern to ensure appropriate packaging or using a device to prevent displacement of the stoppers or plunger seals." *Id.* The Sterilization Examiners maintained the obviousness of terminally sterilizing a prefilled syringe containing an anti-VEGF in view of Metzner and Hasegawa.

114. The Novartis applicant responded to the third office action on January 14, 2014. The applicant continued to argue that the terminal sterilization subject matter was not obvious in view of Metzner and Hasegawa. The response was signed by Individual #3.

115. In a fourth office action on February 7, 2014, the Sterilization Examiners issued a final rejection. The Sterilization Examiners considered the new arguments from the January 14, 2014 response, and maintained that the terminal sterilization subject matter was obvious in view of Metzner and Hasegawa.

116. The Novartis applicant responded to the fourth office action on March 13, 2014. The applicant amended the claims to require that the prefilled syringe surface is decontaminated "to a sterility assurance level of at least 10^{-6}" and argued again that the terminal sterilization subject matter was not obvious in view of Metzner and Hasegawa. The March 13, 2014 response was signed by Individual #3.

117. In a fifth office action on April 2, 2014, the Sterilization Examiners issued a non-final rejection. The Sterilization Examiners detailed a rejection based on Metzner in view of Hasegawa and U.S. Patent No. 5,037,623 ("Schneider"). The Sterilization Examiners explained that Metzner "is not in contact with the prefilled syringe long enough to cause a sterility assurance

level of 10^{-6} (a common standard for sterility) but that the subject matter was still obvious because "[a] person of ordinary skill in the art at the time of the invention would have found it obvious to have achieved a sterility assurance level of at least 10^{-6} in order to have a properly and effectively sterilized medical device (prefilled syringe)." 4/2/14 Office Action at 2, 4. Thus, the Sterilization Examiners maintained that the terminal sterilization subject matter was obvious and not patentable.

118. The Novartis applicant did not respond to the fifth office action. On November 6, 2014, the Sterilization Examiners issued a Notice of Abandonment based on the failure of the Novartis applicant to timely reply to the fifth office action.

119. Individuals #1, #2, and #3, unable to convince the Sterilization Examiners that the terminal sterilization of a prefilled syringe was non-obvious, pivoted their strategy to the Syringe Examiner, who unlike the Sterilization Examiners, was not in an Art Unit directed to chemical compositions, and accordingly was not familiar with the prior art regarding terminal sterilization. The application that led to the '631 Patent, which the Syringe Examiner was examining, was amended to include the limitation "terminally sterilized" on August 9, 2015, which is ***after*** Individual #1, Individual #2, and Individual #3 had received each of the five office actions from the Sterilization Examiners in the '380 Application rejecting terminal sterilization of a prefilled syringe as being obvious in view of at least Metzner and Hasegawa. It was also ***after*** Individual #1, Individual #2, and Individual #3 had conceded the obviousness of terminally sterilizing a prefilled syringe containing an anti-VEGF to the Sterilization Examiners by abandoning the '380 Application.

iii. <u>The Novartis Applicants and Their Representatives Committed Fraud By Deliberately Withholding Material Prior Art From the Syringe Examiner</u>

120. At least Individual #1 and his representatives Individual #2 and Individual #3 deliberately withheld at least the following material information from the Syringe Examiner: (1)

WO '877; (2) Metzner; (3) Hasegawa; and (4) the five office actions from the Sterilization Examiners during the prosecution of the '380 Application concluding that it was obvious to terminally sterilize a prefilled syringe containing an anti-VEGF, such as ranibizumab.

121. WO '877 is material prior art because the Syringe Examiner would not have allowed any of the claims of the '631 Patent if she had been aware of WO '877. The Syringe Examiner had already determined over the course of four office actions that the prefilled syringe set forth in the claim reproduced below was ***obvious and not allowable***:

> 1. (Previously presented) A pre-filled syringe for intravitreal injection, the syringe comprising a glass body forming a barrel, a stopper and a plunger and containing an ophthalmic solution which comprises a VEGF-antagonist, wherein:
>
> (a) the syringe has a nominal maximum fill volume of between about 0.5ml and about 1ml,
>
> (b) the syringe barrel comprises from about 1µg to 100ug silicone oil,
>
> (c) the VEGF antagonist solution comprises no more than 2 particles >50µm in diameter per ml and
>
> wherein the syringe has a stopper break loose force of less than about 11N.

'352 Application, Claimed Rejected in the Fourth Office Action on 3/20/2015

On July 17, 2015, the applicant amended the above claim to add only the limitation that the prefilled syringe is "terminally sterilized," but did not inform the Syringe Examiner about the existence of WO '877, which is prior art and clearly discloses terminal sterilization of a prefilled syringe containing an anti-VEGF for intravitreal injection. *See* WO '877 at 3:8-11 ("Described herein is a terminal sterilization and surface decontamination treatment of prefilled containers, specifically for sterilization of prefilled containers containing sensitive solutions, such as drug product or biological therapeutics, within secondary packaging."), 9:11-14 ("In one particular embodiment, the drug product is a protein solution, such as ranibizumab (e.g., 6 mg/ml or 10 mg/ml) solution for intravitreal injection."), 20:11-16 ("In the following experiment, prefilled syringes were treated with a vaporized-hydrogen peroxide sterilization treatment in a

chamber…Syringes containing protein solutions treated by VHP were compared to control syringes treated with VHP").

122. WO '877 also discloses limitations set forth in the dependent claims of the '631 Patent: dependent claim 8, which requires "the anti-VEGF antibody is ranibizumab"; dependent claim 9, which requires "the ranibizumab is at a concentration of 10 mg/ml"; dependent claims 17-21, which require "[a] blister pack comprising a prefilled syringe…wherein the syringe has been sterilised using H_2O_2 or EtO…the outer surface of the syringe has ≤ 1 ppm EtO or H_2O_2 residue…the total EtO or H_2O_2 residue found on the outside of the syringe and inside of the blister pack is ≤ 0.1mg…wherein ≤5% of the VEFG antagonist is alkylated…wherein the syringe has been sterilised using EtO or H_2O_2 with a Sterility Assurance Level of at least 10^{-6}." *See* WO '877 at 9:11-14 ("In one embodiment, the drug product is a protein solution, such as ranibizumab (e.g., 6 mg/ml or 10 mg/ml) solution for intravitreal injection."), 10:3-5 ("In one terminal sterilization and surface decontamination of prefilled containers within secondary packaging is carried out by treating surfaces of the prefilled container within secondary packaging with vaporized-hydrogen peroxide"), 9:24-26 ("Suitable secondary packaging includes…blister packs"), 7:10-11 ("required [sterility assurance levels] for health care products are defined to be at least 10^{-6}").

123. At least Individual #1, who is the named inventor of WO '877, and Individuals #2 and #3, who were knowledgeable about WO '877 due to their direct involvement in the prosecution of the '380 Application, knew that WO '877 was material to patentability of any claims relating to terminally sterilizing a prefilled syringe containing a drug product for intravitreal injection, and any claims relating to sterilization using hydrogen peroxide.

124. Metzner and Hasegawa are material prior art because the Syringe Examiner would not have allowed any of the claims of the '631 Patent if she had been aware of Metzner and

Hasegawa and the bases on which the Sterilization Examiners repeatedly rejected the '380 Application. The materiality of Metzner and Hasegawa was detailed in five office actions by the Sterilization Examiners, including the fifth office action to which the Novartis applicant ***did not respond***. As explained by the Sterilization Examiners, "Hasegawa et al. teaches a method of sterilizing a prefilled syringe (medicine filled injector) in secondary packaging…applying vaporized hydrogen peroxide to the surface of the prefilled syringe in secondary packaging and allowing the hydrogen peroxide vapor to remain in contact with the prefilled syringe surface for sufficient time to sterilize the syringe surface (abstract, column 8, lines 38-47, and column 12, lines 13-19)." ('380 Application, fifth office action on April 2, 2014 at 3.) The Sterilization Examiners further explained that the combination of Hasegawa and Metzner "teaches a method of using hydrogen peroxide vapor for sterilizing different proteins in secondary packaging (para [0061]) at 30°C (para [0063]) and teaches that the treatment did not destroy the protein products (para [0076])" and that "[a] person having ordinary skill in the art at the time of the invention would understand that if this method is capable of sterilizing prefilled protein drug products in secondary packaging without causing degradation of the proteins that the method is capable of treating the specific protein ranibizumab." ('380 Application, fifth office action on April 2, 2014 at 5.) Accordingly, Metzner and Hasegawa were material to the terminal sterilization limitation of claim 1 of the '631 Patent, as well as the sterilization limitations of dependent claims 17-21 of the '631 Patent.

125. At least Individuals #1, #2, and #3, who were knowledgeable about Metzner and Hasegawa and the five office actions by the Sterilization Examiners, knew that Metzner and Hasegawa were material to the patentability of any claims relating to terminally sterilizing a

prefilled syringe containing a drug product, and any claims relating to sterilization using hydrogen peroxide.

126. Individuals #1, #2, and #3 deliberately withheld WO '877, Metzner, Hasegawa, and the five office actions by the Sterilization Examiners from the seven information disclosure statements submitted between January 25, 2013 and March 11, 2015 in the application for the '631 Patent. All of these information disclosure statements were submitted after the initial office action rejecting the claims of the '380 Application in view of Metzner and Hasegawa, and while there were dependent claims in the application for the '631 Patent reciting hydrogen peroxide sterilization.

127. Furthermore, eight months after abandoning the '380 Application, having failed in their multi-year effort to convince the Sterilization Examiners of the patentability of a terminally sterilized prefilled syringe for a protein drug product and also having failed for years to convince the Syringe Examiner of the patentability of claims directed towards a syringe barrel having low amounts of silicone oil in the application for the '631 Patent, Individuals #1, #2, and #3 pivoted their strategy. Specifically, the claims in the application for the '631 Patent were amended on July 17, 2015 to include the requirement for a "terminally sterilized" prefilled syringe. But in doing so, Individuals #1, #2, and #3 made another ***deliberate decision not to disclose the very subject matter, i.e., WO '877, Metzner, Hasegawa, and the office actions by the Sterilization Examiners, that they knew demonstrated the amended claims of the '631 Patent were not patentable***.

128. Individuals #1, #2, and #3 knew when claim 1 of the '631 Patent was amended adding the words "terminally sterilized" that the previous two and a half years of examination by the Syringe Examiner had been focused on prior art disclosing the obviousness of using a low amount of silicone oil. They also knew that they had a continuing duty to disclose material

information. That duty required them to update the information presented to the Syringe Examiner to include information material to the patentability of the newly amended claim 1 including the "terminally sterilized" limitation that was added in the July 17, 2015 amendment. Notably, the applicant submitted an information disclosure statement concurrent with the amendment for the '631 Patent on July 17, 2015, and another information disclosure statement on November 17, 2015, identifying new information for the Syringe Examiner to consider, but ***none of the references submitted in the two new information disclosure statements were prior art describing terminal sterilization of a prefilled syringe, prior art that they were well aware of from the prosecution of the '380 Application***. Instead, the applicant continued to submit prior art regarding siliconization of syringes, while withholding material prior art – WO '877, Metzner and Hasegawa – disclosing terminal sterilization of prefilled syringes. For example, the July 17, 2015, information disclosure statement included the following non-patent literature citations regarding siliconization:

	1	CHAN ET AL: "Syringe Siliconization Process Investigation and Optimization" Journal of Pharmaceutical Science and Technology, Issue 66, pp.137, 147-148, March 2012	☐
	2	LANKERS: "The Relationship Between Silicone Layer Thickness, Free Silicone Oil and Protein Aggregation In Prefilled Syringes" 2010 AAPS National Biotechnology Conference San Francisco, Slides 25, 39, 46, mAY 19, 2010	☐
	3	MAJUMDAR ET AL: " Evaluation of the Effect of Syringe Surfaces on Protein Formulations" Journal of Pharmaceutical Sciences, Issue 100, pp.2563-2573, July 2011	☐
	4	BAKRI AND EKDAWI: "Intravitreal Silicone Oil Droplets after Intravitreal Drug Injections" Retina, Issue 28, pp.996-1001, July 2008	☐

Excerpt from '352 Application, July 17, 2015 Information Disclosure Statement

Indeed, WO '877, Metzner and Hasegawa were not cumulative of *any* of the art disclosed throughout prosecution. Thus, although Individuals #1, #2, and #3 knew that they had a continued duty to submit information to the Syringe Examiner, and knew that terminal sterilization was of particular relevance given the addition of that limitation to claim 1, they failed to submit the material prior art regarding terminal sterilization of a prefilled syringe that they knew of from the

prosecution of the ’380 Application—i.e., WO ’877, Metzner, Hasegawa, and the five office actions by the Sterilization Examiners.

129. Therefore, at the time of the July 17, 2015 amendment in the application resulting in the ’631 Patent, and the Syringe Examiner’s August 19, 2015 notice of allowance, at least Individuals #1, #2, and #3 knew of and deliberately withheld: (i) WO ’877; (ii) Metzner; (iii) Hasegawa; (iv) the five office actions by the Sterilization Examiners regarding obviousness of terminally sterilizing a prefilled syringe containing an anti-VEGF; and (v) their own admission of obviousness of that subject matter based on the failure to respond to the fifth office action in the ’380 Application and the resulting abandonment of the ’380 Application. The single most reasonable inference that may be drawn from this evidence is that at least Individuals #1, #2, and #3 made a ***deliberate choice to deceive the USPTO by withholding the prior art that they knew disclosed terminal sterilization and was highly material*** to the pending claims in the application leading to the ’631 Patent. The deception was successful, and the Syringe Examiner, not knowing that terminal sterilization of a prefilled syringe containing an anti-VEGF was fully disclosed and obvious in view of the prior art, allowed the application which issued as the ’631 Patent.

130. Upon information and belief, Individuals #1, #2, and #3 were motivated to deceive the USPTO in order for their employer Novartis to maintain or establish dominance in the market for prefilled syringes containing VEGF antagonist. Indeed, Novartis had repeatedly threatened to enforce the fraudulently procured ’631 Patent against Regeneron and demanded that Regeneron take a license to the application before the ’631 Patent even issued, thereby attempting to delay and deter Regeneron’s EYLEA PFS launch and forcing Regeneron to incur additional costs to defend against these unenforceable patent claims. Following the EYLEA PFS launch in late 2019,

Novartis filed suit against Regeneron on June 19, 2020, alleging that EYLEA PFS infringes the fraudulently procured and unenforceable claims of the '631 Patent.

G. Novartis's and Vetter's Overarching Conspiracy to Unreasonably Restrain Competition in the Anti-VEGF PFS Market

131. Novartis and Vetter have used their supposed ownership dispute over the fraudulently procured '631 Patent to enter into a "settlement" that was, in effect, an anticompetitive agreement designed to control—and limit—the supply of anti-VEGF PFS treatments for ophthalmic diseases in the United States. As part of this overarching conspiracy, Novartis and Vetter have tried to frustrate and delay Regeneron's entry into the U.S. anti-VEGF PFS market and to artificially raise Regeneron's costs so as to ensure that Novartis's LUCENTIS PFS (and eventually BEOVU PFS) effectively remain the only FDA-approved anti-VEGF PFS in the market.

i. Regeneron/Vetter Collaboration on the EYLEA PFS

132. Vetter is one of a small number of "fillers" with the assets, capabilities, and scale to fill syringes with complex biologic drug products like EYLEA under the required sterile conditions. Commercializing these PFS has unique challenges and requirements involving, among other things, regulatory approvals and the need for specialized equipment and filling lines possessed by a very limited number of firms. Vetter is a leading global supplier in this field, including for the United States. The United States is a significant market for Vetter, and its market strategy is directly aimed at ensuring success in the United States. According to Vetter, "[a]round 90 percent of [their] prefilled drug-delivery systems," which include PFS, "are sold abroad. Vetter's major customers are in the USA where they constitute a market share of more than 50 percent [sic]."[60] Indeed, upon information and belief, Vetter is the exclusive filler of LUCENTIS

[60] Interview, "Vetter – A World Market Leader," Healthcare Industry BW (Oct. 14, 2011), *available*

PFS and Vetter will be the filler for Novartis's BEOVU PFS as well if the FDA approves it. Due to its experience and capabilities, Vetter is a uniquely important filler for anti-VEGFs, especially for PFS used to treat certain ophthalmic diseases.

133. Regeneron and Vetter have a long-standing relationship that well predates Novartis filing for the application that became the '631 Patent. Vetter is a long-term filler for EYLEA vials on a non-exclusive basis. And, significantly, starting in 2005, Regeneron and Vetter collaborated to commercialize an EYLEA PFS. During the course of their collaboration, Vetter filled its first EYLEA PFS for Regeneron in 2007 and thereafter continued to fill EYLEA PFS for Regeneron's use in various clinical trials and for other testing purposes. Vetter also worked with Regeneron to develop an EYLEA PFS for the Australian market, and an EYLEA PFS was approved by the Australian Therapeutic Goods Administration at least by March 7, 2012—all prior to Novartis filing its application for the '631 Patent.

ii. Novartis/Vetter's Anticompetitive Agreement and Vetter's Abrupt Change in Demands to Regeneron

134. Notwithstanding Vetter's collaboration with Regeneron to commercialize an EYLEA PFS, and unknown to Regeneron, Vetter and Novartis were vying for ownership to the application underlying the '631 Patent. Vetter and Novartis ultimately settled by entering into an arrangement in 2013. But this was no ordinary settlement of a patent dispute. Instead, Novartis's and Vetter's "settlement" was a pretext for an unlawful conspiracy to control the supply of, and thus restrain competition for, anti-VEGF PFS treatments in the United States. Novartis ultimately used the process to obtain control and influence over Vetter's PFS filling services so that it could inhibit its rivals in the anti-VEGF PFS market—like Regeneron.

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at https://www.gesundheitsindustrie-bw.de/en/article/news/vetter-a-world-market-leader-we-put-ourselves-in-our-clients-shoes.

135. Upon information and belief, Novartis provided Vetter with a "co-exclusive" license to its fraudulently procured '631 Patent in exchange for Novartis extracting a lucrative financial stake in Vetter's PFS filling services. This anticompetitive agreement co-opted Vetter, allowing Novartis to exert influence over Vetter's current and future PFS customer relationships. Novartis was assured that any of Vetter's existing customers—notably Regeneron—would be required to immediately take a sublicense to the pending application for the '631 Patent with conditions that were highly favorable to Novartis: (1) a long-term, exclusive supply relationship with the firm that fills LUCENTIS PFS; and (2) a commitment never to challenge Novartis's '631 Patent if and when it issued. Vetter was induced to enter into this agreement because Novartis offered, at a minimum, the potential that customers like Regeneron would be forced into long-term, exclusive contracts with Vetter for PFS filling services under the threat of an infringement suit by Novartis. In short, Novartis stood to benefit from the conspiracy by controlling the entire U.S. anti-VEGF PFS market while Vetter stood to benefit by becoming the sole filler for the U.S. anti-VEGF PFS market.

136. Following its agreement with Novartis, Vetter ***abruptly reversed course*** in late 2013 and started implementing Novartis's plan to limit competition. Despite having collaborated with Regeneron to commercialize EYLEA PFS for approximately eight years, Vetter contacted Regeneron, claiming that Novartis had a ***pending patent application*** covering EYLEA PFS and demanding that Regeneron now take a license to the yet to be issued patent to continue development. In October 2013, Vetter sent a sublicense demand to Regeneron for the application that would eventually become Novartis's '631 Patent, referencing the agreement between Novartis and Vetter relating to Vetter's existing customers.

137. Vetter's demand to Regeneron was alarming not only because it represented an

about-face by Vetter, but also because it tried to impose radical and onerous terms on Regeneron. First, Vetter suddenly demanded that Regeneron use Vetter as the ***exclusive EYLEA PFS filler for nearly 20 years***. This demand not only represented a complete departure from its collaboration with Regeneron on the EYLEA PFS, but it also was in stark contrast to Vetter's commercial relationship with Regeneron for EYLEA vials. Vetter has filled, and continues to fill, EYLEA vials ***without*** exclusivity—much less a demand for 20 years of exclusivity. Given that Vetter is a leading PFS filler and Regeneron had few options, it was important for Regeneron to continue working with Vetter on the EYLEA PFS that was already underway for approximately eight years. But Regeneron could not tolerate being locked into a 20-year exclusive filler arrangement that would only constrain the ability of EYLEA PFS to compete against Novartis's products.

138. Given Vetter's agreement and relationship with Novartis, Vetter's loyalty is divided at best. Vetter is the exclusive PFS filler for LUCENTIS, and upon information and belief, Vetter also will be the exclusive PFS filler for BEOVU. Vetter will be responsible for filling both anti-VEGF products connected to Novartis. And had Regeneron agreed to Vetter's demand for an exclusive, long-term contract, then Vetter and Novartis would have controlled the supply of every single anti-VEGF PFS globally for the treatment of certain ophthalmic diseases. Vetter only has finite resources and capacity, and Regeneron was concerned that Novartis's PFS products would take priority over EYLEA PFS given their underlying conspiracy. Limiting the supply of EYLEA PFS would artificially inflate sales of LUCENTIS PFS (and later BEOVU PFS), all to the benefit of Novartis. Tellingly, Vetter refused to provide any assurances whatsoever that it could meet Regeneron's projected EYLEA PFS demand or to allow Regeneron to use alternative PFS filling services in the event that Vetter was capacity-constrained. Regeneron had every reason to be concerned that Novartis and Vetter would use this forced exclusivity to strangle EYLEA PFS.

139. Regeneron's concerns about exclusivity were only exacerbated by Vetter's quality control issues. Regeneron's work with Vetter revealed another concern about committing to a long-term, exclusive filling arrangement. While collaborating with Vetter on the EYLEA PFS, Regeneron had conducted various testing and clinical trials on numerous batches filled by Vetter. In 2013, Regeneron identified some quality and performance issues with Vetter's PFS batches. Regeneron voiced these concerns to Vetter about the filling lines. With Vetter in league with Novartis, Regeneron had legitimate concerns that Vetter would not address these or future quality issues expeditiously, if at all.

140. Separate and apart from the demand for 20 years of exclusivity, Vetter's sublicense contained an unlawful "no-challenge" clause mandating that Regeneron ***never challenge the validity*** of Novartis's fraudulently procured '631 Patent. The offer explicitly stated that the sublicense would immediately terminate if Regeneron—or any customer—ever "challenge[d], or intentionally assist[ed] any third party in challenging, the validity of any rights" for Novartis's '631 Patent. Regeneron could not, and would not, accept this no-challenge provision in view of its own work in developing an EYLEA PFS, as well as the extensive prior art in the space showing that the PFS that Novartis purported to claim was not patentable. Vetter and Novartis refused to provide Regeneron with a sublicense on any other terms.

141. These demands to Regeneron were just one facet of the overarching conspiracy between Novartis and Vetter expressly aimed at controlling the total supply of all anti-VEGF PFS treatments for certain ophthalmic diseases. They had jointly agreed to leverage Novartis's fraudulently procured '631 Patent to try to coerce Regeneron—and any future competitors—into long-term exclusive PFS filling relationships on the threat of a bogus patent infringement lawsuit.

iii. Novartis/Vetter's Concerted Denial of Access to PFS Filling Services

142. After several rounds of negotiations with Vetter over the sublicense and attempts to find a middle ground on the onerous terms that Vetter had now tied to continuing its work on EYLEA PFS, it became clear to Regeneron that Vetter—operating at the behest of Novartis—was forcing Regeneron to make a Hobson's choice:

(A) Accede to Novartis's and Vetter's demand that Vetter be the exclusive EYLEA PFS filler for nearly 20 years—accepting the supply, capacity, and quality risks that had raised concerns—and never challenge Novartis's fraudulently procured '631 Patent in exchange for a sublicense; or

(B) Lose the option of using Vetter (a leading PFS filler with unique capabilities, a pre-existing collaboration, and development history spanning approximately eight years) as Regeneron's PFS supplier altogether, accept the resulting delay in launching EYLEA PFS, ***and*** likely face a bogus patent infringement lawsuit from Novartis seeking to block Regeneron from selling EYLEA PFS in the United States.

143. Given that Vetter and Novartis conditioned a sublicense to the '631 Patent on a long-term exclusive deal with Vetter and an unlawful "no-challenge" clause, it is reasonable to infer that Novartis viewed the onerous terms that Vetter demanded from Regeneron (or the alternative, a severance of the Vetter/Regeneron relationship) as providing significant economic value. With Vetter's and Novartis's interests joined by the '631 Patent, locking Regeneron into a long-term contract with its co-conspirator would allow Novartis to control the supply of effectively all FDA-approved anti-VEGF PFS treatments for ophthalmic diseases. Novartis also would benefit from the limited supply, and thus limited availability, of EYLEA PFS. And given the unlawful "no challenge" clause in the sublicense, the practical effect was to ensure that Regeneron could not use

an alternative PFS filler for EYLEA PFS under any circumstances or face a bogus patent infringement lawsuit from Novartis. Vetter, for its part, stood to benefit economically had Regeneron been willing to submit to its demand for a long-term, exclusive supply arrangement.

144. Regeneron had no choice but to refuse Novartis's and Vetter's unlawful demands because Regeneron knew that the exclusive Vetter arrangement would ultimately compromise the competitiveness of EYLEA PFS. Regeneron rejected what was essentially an all-or-nothing offer from Vetter, even though it knew that doing so would delay the launch of EYLEA PFS and cost Regeneron millions of dollars in unnecessary costs.

145. In retaliation, Novartis and Vetter punished Regeneron. Unable to control the supply of EYLEA PFS through Vetter, they jointly agreed to ***cut off Regeneron entirely***. Defendants denied Regeneron access to any of Vetter's PFS filling services for EYLEA. Upon information and belief, Vetter and Novartis knew that it would be difficult, expensive, and time-consuming for Regeneron to find, switch to, qualify, and ramp up for commercialization with an alternative filling and supply chain for EYLEA PFS—especially once Vetter stopped providing any filling. That is precisely what happened. Having refused to become a pawn in Novartis's and Vetter's anticompetitive scheme, Regeneron was forced to invest significant time, money, and effort to establish a new, reliable supply chain for EYLEA PFS. Regeneron had to find another potential PFS filler, modify the filler's equipment, perform qualification testing, and conduct a validation process just to get the PFS filling process up and running on a consistent and quality basis. Regeneron then had to obtain FDA approval for this new version of EYLEA PFS, including the underlying components and specific supply chain. All of these additional steps ultimately delayed Regeneron's EYLEA PFS launch by years.

146. In late 2017, Regeneron had renewed discussions with Vetter regarding the '631 Patent. Vetter once again sent the Novartis sublicense offer that was provided in 2013, reaffirming its earlier demand. Regeneron could only receive a sublicense to Novartis's '631 Patent if it accepted Vetter's exclusive supply terms. But as explained above, such an unlawful exclusive agreement with Vetter would constrain supply of anti-VEGF PFS treatments—specifically Regeneron's EYLEA PFS—resulting in reduced quality, reduced innovation, and reduced choice for U.S. patients. Regeneron had no choice but to refuse this offer again in 2017.

147. Regeneron's legitimate business concerns with a long-term, exclusive contract with Vetter for EYLEA PFS appear to have been borne out in Europe by the delayed launch of EYLEA PFS. Bayer received approval from the European Medicines Agency to market EYLEA PFS in the European Union in 2012.[61] However, upon information and belief, Vetter successfully imposed the unreasonable exclusive supply restrictions on Bayer that Regeneron rejected. Given that EYLEA PFS did not launch in Europe until ***eight years later in 2020***, the reasonable inference is that Vetter had been unable to adequately supply quality PFS filling services for EYLEA PFS in Europe because Vetter had prioritized LUCENTIS PFS over EYLEA PFS, ultimately focusing its time, money, and development efforts on Novartis's drug product. The result harmed physicians and patients who had no access to EYLEA PFS in European markets for eight years despite the product have received regulatory approval.

H. Novartis's Continued Efforts to Artificially Limit Competition from Regeneron

148. Consistent with its anticompetitive conspiracy with Roche involving LUCENTIS in the European Union, and in furtherance of its U.S. conspiracy with Vetter, Novartis has engaged

[61] European Medicines Agency, EYLEA, "Assessment Report," (Sept. 20, 2012), *available at* https://www.ema.europa.eu/en/documents/assessment-report/eylea-epar-public-assessment-report_en.pdf.

in all efforts to unlawfully block, or at least hinder, competition from Regeneron's EYLEA PFS in the United States in a bid to control the anti-VEGF PFS market.

149. In 2018, Novartis made its first attempt to misuse patent litigation in order to eliminate competition from EYLEA by filing a lawsuit in the Southern District of New York, asserting that Regeneron infringed a different Novartis patent, U.S. Patent No. 5,688,688. That effort failed when the Court entered a Judgment of Noninfringement and dismissed Novartis's claims with prejudice.[62]

150. More recently, Novartis engaged in allegedly unlawful and dangerous conduct with respect to its most recent anti-VEGF to reach the market, BEOVU. BEOVU is a Novartis-owned anti-VEGF that Novartis had been working to develop for years, including conducting clinical trials comparing the safety and efficacy of BEOVU to EYLEA. Novartis had been lauding BEOVU as a new, groundbreaking, and blockbuster anti-VEGF for the treatment of wet AMD. Novartis's clinical trials, however, uncovered significant safety issues in patients treated with BEOVU, including higher rates of severe adverse reactions such as IOI, RAO, and ORV that could cause ***permanent blindness***. Rather than disclose these elevated risks, Novartis instead hid critical safety data from the public—and from the FDA[63]—and embarked on a promotional campaign during its 2019 launch falsely touting BEOVU to be as safe as EYLEA. Despite being well aware of the

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[62] *See Novartis Vaccines and Diagnostics, Inc. et al v. Regeneron Pharmaceuticals Inc.*, No. 1:18-cv-02434, Judgment of Noninfringement and Order of Dismissal, Dkt. 305 (S.D.N.Y. Sept. 4, 2019).

[63] Consistent with these allegations, a complaint for wrongful termination was recently filed by a former Novartis employee alleging that Novartis deliberately concealed critical safety information for BEOVU. *See Butuner v. Novartis Pharmaceuticals Corp.*, No. 2:19-cv-06590, Complaint, Dkt. 1 (D.N.J Feb. 22, 2019). According to the complaint, Novartis executives knowingly refused to publish true IOI rates in 2018, which they knew to be much higher than EYLEA's rates. *See id.* at ¶¶ 28-32. The complaint also alleges that Novartis failed to adequately correct a material error in the safety data that it reported on arterio thromboembolic event rates, which were falsely reported as superior to EYLEA. *See id.*

increased safety risks associated with BEOVU, Novartis tried to steer physicians and patients away from Regeneron's tried and true EYLEA and towards its own BEOVU, which has significant safety issues.

151. Shortly after BEOVU launched in October 2019, physicians quickly learned what Novartis had tried to hide. BEOVU patients suffered from a growing number of serious adverse reactions, including the IOI, RAO, and ORV events seen in Novartis's clinical trials. Following a series of stern public warnings from the American Society of Retinal Specialists and a significant outcry from U.S. physicians and patients, Novartis commissioned an external safety review of BEOVU. After the results of that review undeniably confirmed the safety issues associated with BEOVU, Novartis was forced to update its FDA-approved label, highlighting the severity and incidence of adverse reactions that could cause blindness in patients. Novartis also was forced to admit that the adverse reactions of RAO and ORV caused by BEOVU "are part of a spectrum of intraocular inflammation rates" revealed during Novartis's pre-launch clinical trials.[64]

152. Given that Novartis's attempts to compete on the merits against EYLEA with BEOVU failed miserably, Novartis has fallen back on its fraudulently procured '631 Patent and its conspiracy with Vetter in a last ditch effort to again try to stop Regeneron from selling EYLEA PFS in the United States. For years, Novartis has operated through Vetter to issue threats to enforce the '631 Patent against Regeneron and EYLEA PFS. Now Novartis is doing it directly.

153. On June 19, 2020, Novartis committed the latest step in its conspiracy with Vetter to foreclose Regeneron and undermine the competitiveness of EYLEA PFS, and its own attempt

[64] Press Release, Novartis, "U.S. FDA Approves Updated Novartis Beovu® Label To Include Additional Safety Information" (June 11, 2020), *available at* https://www.novartis.com/news/media-releases/us-fda-approves-updated-novartis-beovu-label-include-additional-safety-information#:~:text=Basel%2C%20June%2011%2C%202020%20%E2%80%94,and%20retinal%20vascular%20occlusion1.

monopolize the anti-VEGF PFS market. Novartis sued Regeneron in the ITC and the NDNY, alleging patent infringement of its fraudulently procured '631 Patent to wrongfully exclude importation of EYLEA PFS and/or components thereof and enjoin EYLEA PFS sales. The timing could not be more suspect. Novartis did not file suit when EYLEA PFS was approved by FDA, or even when Regeneron launched EYLEA PFS in the United States. Instead, Novartis waited until more than six months had passed—when Regeneron's roll out of EYLEA PFS was highly successful and almost complete with approximately 80% of patients switched from EYLEA vials to PFS ***and*** when BEOVU's clinical safety issues came to light. The only conclusion is that this second infringement lawsuit against Regeneron is just a desperate and unlawful attempt by Novartis to salvage its BEOVU failure.

154. Once again, Novartis is trying to wrongfully stop physicians and patients from accessing what has been viewed as a superior treatment—EYLEA—in a more accurate and more convenient method of administration—PFS. If Novartis somehow manages to succeed, it will deprive patients and physicians of EYLEA PFS and all of its benefits, forcing them to choose between a less effective treatment that requires more frequent injections into a patient's eye (LUCENTIS PFS), Novartis's newest treatment that places patients at risk of serious adverse reactions and even blindness (BEOVU), or EYLEA in a less convenient and less preferred format.

155. Even if Novartis does not succeed in its ITC and NDNY actions, it may well succeed in dampening demand for EYLEA PFS and distracting Regeneron from competing aggressively in the anti-VEGF PFS market. Physicians are reluctant to switch a patient's treatment regimen, so much so that for new patients some physicians may now opt for LUCENTIS PFS over EYLEA PFS, despite its considerable drawbacks, simply because there is a risk that EYLEA PFS may be forced out of the market. This reluctance would have the effect of reducing demand for

EYLEA PFS and artificially inflating sales of LUCENTIS PFS (and perhaps BEOVU PFS, if approved prior to a decision on Novartis's patent infringement claims). Novartis's ITC and NDNY actions may also have the effect of forcing Regeneron to invest in a contingent source of supply and production for EYLEA in vial form—an outcome that Novartis itself told the ITC that Regeneron should contemplate: "[T]o the extent Regeneron is truly concerned about its ability to supply patients with the vial presentation at the conclusion of this investigation, it is a problem … it can easily rectify by beginning the process of converting to the vial today."[65] This glib suggestion underscores Novartis's complete lack of concern for the competitive and commercial consequences of filing actions asserting its fraudulently obtained '631 Patent.

RELEVANT MARKET

156. The relevant product market is anti-VEGFs in prefilled syringes that are approved by the FDA for the treatment of certain ophthalmic diseases—referred to as the "anti-VEGF PFS" market.

157. As explained above, anti-VEGFs are a class of FDA-approved drugs that are publicly recognized in the medical community as the standard of care for treating certain ophthalmic diseases, including Wet Age-Related Macular Degeneration, Diabetic Retinopathy, Diabetic Macular Edema, and Macular Edema following Retinal Vein Occlusion. No other FDA-approved treatment is reasonably interchangeable with anti-VEGFs for the treatment of these ophthalmic diseases.

158. Drugs used "off-label" for the treatment of ophthalmic diseases are also not reasonably interchangeable with FDA-approved anti-VEGFs. These off-label treatments have

[65] *See Certain Pre-Filled Syringes for Intravitreal Injection and Components Thereof*, DN 3460, USITC No. 337-TA-[__], Complainants' Reply to Statements on the Public Interest, at 2 (July 9, 2020) (the "Novartis ITC Reply").

distinct characteristics and uses based upon their FDA-approved indications. As discussed above in ¶¶ 66-68, drugs like Avastin need to be repackaged by third parties before they can be administered intravitreally to patients. Due to concerns with dosing accuracy and sterilization, many ophthalmologists and retinal specialists are unwilling to prescribe Avastin off-label to their patients. Off-label drugs also have shown to be less effective at treating certain ophthalmic diseases. Nevertheless, some practitioners, often due to the constraints imposed by insurance payers, attempt to treat patients with Avastin first before ever considering treatment with anti-VEGFs that are FDA approved for ophthalmic conditions. Thus, even for the practitioners that do first use Avastin, Avastin is not reasonably interchangeable with anti-VEGFs FDA-approved for ophthalmic diseases because the possibility of using Avastin has already been exhausted.

159. Additionally, non-FDA approved treatments, like Avastin, do not constrain the pricing of FDA-approved anti-VEGF treatments for ophthalmic diseases. Avastin, a cancer drug, is priced relative to other cancer drugs, not ophthalmic treatments, and is far less expensive (approximately $50 per dose) than FDA-approved anti-VEGF ophthalmic treatments (approximately $1,500 to $2,000 per dose). The fact that FDA-approved anti-VEGF treatments for ophthalmic diseases have distinct prices from, and are able to sustain such a significant premium over, Avastin demonstrates that they comprise a distinct relevant product market. A small, but significant, price increase in FDA-approved anti-VEGF PFS treatments for ophthalmic diseases therefore would not divert meaningful sales to Avastin or any other products.

160. Consistent with industry recognition and other practical indicia, Novartis does not consider Avastin to be a competitor to EYLEA PFS and LUCENTIS PFS. In its Public Interest Statement filed in its ITC action, Novartis did not even mention Avastin as a potential alternative

treatment for patients to use.[66] Drugs like Avastin that are not FDA-approved to treat ophthalmic diseases are accordingly not part of the relevant product market.

161. In addition, anti-VEGF PFS treatments do not meaningfully compete with anti-VEGF vials given that they each have particular characteristics and uses. As a result of their method of administration, anti-VEGF PFS have distinct advantages in terms of accuracy and convenience, which differentiates them from anti-VEGFs approved by the FDA in vial form—even those containing the same active drug ingredient. Novartis itself recognizes the benefits of convenience and efficiency for PFS in its Public Interest Statement to the ITC, referring to it as "an important and valuable advance."[67] Tellingly, physicians have almost completely converted their patients from vials to PFS due to the substantial benefits of PFS. Vials are becoming an outdated method of administration as patients and physicians recognize the substantial benefits in shifting permanently from vials to PFS.

162. As discussed above in ¶¶ 71-84, PFS are quicker and easier to use than vials for anti-VEGFs. They eliminate multiple steps in the process, reducing the risk of inaccurate dosing and increasing patient comfort. Studies also show that cases of endophthalmitis, an inflammation of the interior of the eye, may be reduced with the use of anti-VEGFs in PFS instead of vials.[68] In fact, some third-party analysts "anticipate that a prefilled syringe will decrease the chance for endophthalmitis ***by 50%***."[69] By reducing the number of necessary steps for preparation and

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[66] *See id.* Nor did Novartis mention Macugen as a potential alternative for patients to use. *See id.* While Macugen received FDA approval in 2004 for a prefilled syringe to treat wet AMD only, it is also an older, less effective treatment that is rarely prescribed anymore, if at all.

[67] *See* Novartis ITC Reply, at 3.

[68] Storey PP, Tauqeer Z, Yonekawa Y, et al., "The Impact of Prefilled Syringes on Endophthalmitis Following Intravitreal Injection of Ranibizumab," Am J Ophthalmol; 2019;199:200-208; doi:10.1016/j.ajo.2018.11.023.

[69] Biotechnology Quarterly, "Regeneron Pharmaceuticals: Bullish on Dupixent but EYLEA Facing

administration, PFS result in less exposure to potential contaminants that may cause adverse reactions or complications during injection.

163. In addition to cross-elasticity of demand, other practical indicia demonstrate that anti-VEGF PFS are not reasonably interchangeable with anti-VEGF vials. Industry participants, including retinal specialists, recognize the significant advantages of PFS over vials: "Using syringes prefilled with the soluble anti-VEGF agents will protect patients from the disastrous consequences of endophthalmitis, assure the most efficient manner of precise dosing, and assist with patient flow in growing, busy clinics."[70] Similarly, a third-party survey shows that a significant number of doctors have indicated that they will increase their prescribing of EYLEA due to the availability of PFS.[71] And Genentech and Novartis have publicly touted the benefits of LUCENTIS PFS compared to LUCENTIS vial.

164. Furthermore, manufacturing and commercializing anti-VEGF PFS requires unique production facilities and capabilities that are distinct from those required to manufacture anti-VEGF vials. It involves, among other things, specialized equipment and filling lines possessed by a limited number of firms, as well as separate regulatory approval for anti-VEGF PFS treatments.

165. The benefits of PFS are also evidenced by the rapid uptake of PFS following launch. Recent examples indicate that approximately 80% of patients changed over from vial to PFS shortly after an anti-VEGF PFS was introduced. The experiences with both LUCENTIS PFS and

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Major Competitive Threats" (Feb. 2020), at 19.

[70] Michael Colucciello, M.D., "Prefilled Syringe Delivery of Intravitreal Anti-VEGF Medications: Advantages for Patients and Physicians, *Retinal Physician* (Mar. 1, 2019), *available at* https://www.retinalphysician.com/issues/2019/march-2019/prefilled-syringe-delivery-of-intravitreal-anti-ve#reference-15.

[71] *See, e.g.*, Piper Sandler, "For Beovu, Surveys Indicate It Was the Best of Times, Then the Worst of Times" (Mar. 3, 2020), at 18.

EYLEA PFS demonstrate the strong preference of physicians for PFS over vials. And a small, but significant, price increase in the PFS version would not cause physicians to substitute the vial version for PFS (even if they contain the same underlying anti-VEGF).

166. The relevant geographic market is the United States. Because FDA approval is required for the import, export, sale, and distribution of these complex biologic products in the United States, patients and physicians cannot turn to sellers outside the United States for these drug products. Neither physicians nor patients can import non-FDA-approved anti-VEGFs for the treatment of ophthalmic diseases in response to small, but significant, price increases.

167. FDA-approved anti-VEGF PFS are also sold throughout the United States as people who suffer from ophthalmic diseases live across the country. Finally, pricing for anti-VEGF PFS treatments is done on a national basis.

MONOPOLY POWER

168. Prior to the recent launch of EYLEA PFS, LUCENTIS PFS possessed virtually 100% of the U.S. market for anti-VEGFs in PFS approved by the FDA for the treatment of certain ophthalmic diseases. LUCENTIS PFS has possessed this monopoly power since its 2017 U.S. launch. LUCENTIS PFS currently has a significant share of the market. If Novartis succeeds in enjoining Regeneron's EYLEA PFS through its ITC action, then Novartis's LUCENTIS PFS will once again be the only available anti-VEGF PFS approved by the FDA and therefore will revert to having virtually 100% share of the anti-VEGF PFS market in the United States.

169. Novartis has possessed, and will again possess if it succeeds in enjoining EYLEA PFS, monopoly power in the anti-VEGF PFS market. LUCENTIS PFS' significant and durable market share is attributable to Novartis as the co-developer and co-owner of LUCENTIS and LUCENTIS PFS, as well as Novartis being the '631 Patent holder and licensor to Genentech.

Novartis's license to Genentech for the '631 Patent enables Genentech to sell LUCENTIS PFS in the United States. Novartis also owns a 33.3% stake in Roche, the parent company of Genentech. Novartis accordingly benefits significantly from LUCENTIS PFS dominating the anti-VEGF PFS market in the United States.

170. Novartis has attempted to maintained, and then attempted to reacquire, its monopoly power in the anti-VEGF PFS market through its collusive agreement with Vetter, which enables Novartis to control Vetter's PFS filling services and customer relationships. With capacity constraints and other hurdles to commercializing an anti-VEGF PFS, and Vetter exclusively filling LUCENTIS PFS, Novartis has a tight grip on the supply of these drug products. Vetter also has attempted to re-monopolize the market by enforcing its fraudulently procured '631 Patent against Regeneron.

BARRIERS TO ENTRY

171. The anti-VEGF PFS market in the United States is characterized by substantial and durable barriers to entry that protect and fortify Novartis's monopoly power, and the monopoly power Novartis is attempting to re-acquire, by asserting the fraudulently procured '631 Patent against Regeneron.

172. Barriers to entry include the substantial time and expenses required to develop a complex and innovative biologic drug like an anti-VEGF PFS. Barriers to entry also include FDA's regulatory and approval process, which requires significant time, investment, and efforts to obtain U.S. approval for any pharmaceutical product. For example, the FDA recently rejected an application from a potential entrant for a new anti-VEGF therapy to treat wet AMD due to concerns with safety risks, including high incidence of intraocular inflammation.[72] The FDA approval

[72] "Allergan/Abbvie's Macular Degeneration Drug Rejected by FDA," BioSpace (June 26, 2020), *available at* https://www.biospace.com/article/fda-reject-s-allergan-s-abicipar-pegol-for-age-related-

process for a PFS version alone is sufficiently substantial that it effectively insulates the anti-VEGF PFS market from new entry even for a firm that already has an FDA-approved anti-VEGF drug product.

173. Even after a company develops an anti-VEGF PFS and obtains FDA approval, there are substantial barriers to bringing it to market. The company must secure a reliable multi-level supply chain, including a filler for the PFS. Vetter is the dominant PFS filler, there are limited other fillers available, and entry and expansion in the filling space is rare. As explained by Vetter, "the creation of…a commercial site for manufacturing pharmaceutical and biotech drug products requires a significant initial investment of more than $300 million. . . .Therefore, in order to seriously undertake such a large project, it is important that [they] have in place a stable financial plan that justifies this investment."[73] Regeneron's own experience in developing EYLEA PFS and in establishing a new supply chain once Vetter refused to continue development confirms that it takes many years and millions of dollars to secure a viable alternative PFS filler.

174. Finally, through their anticompetitive and exclusionary conduct, Defendants have erected, and Novartis continues to raise with its fraudulent patent infringement suit, additional, artificial and anticompetitive barriers to entry in the U.S. anti-VEGF PFS market. Any prospective entrant into the anti-VEGF PFS market, including any anti-VEGF PFS biosimilar, would have to contend with the same threats that Vetter and Novartis have levied against Regeneron.

ANTITRUST INJURY

175. By their anticompetitive scheme, Defendants Novartis and Vetter have harmed—

macular-degeneration/.

[73] FiercePharma, "Start of Vetter's $300M U.S. Sterile Plant Project Delayed for Years," (Feb. 6, 2018), *available at* https://www.fiercepharma.com/manufacturing/ground-breaking-for-vetter-u-s-manufacturing-plant-may-not-happen-until-2022.

and continue to harm—competition in the U.S. anti-VEGF PFS market in violation of Sections 1 and 2 of the Sherman Act. As a result, Regeneron has suffered and will continue to suffer injury to its business or property, including incurring substantial additional costs in the manufacturing and commercialization of EYLEA PFS, defending against Novartis's bogus patent infringement actions in the NDNY and ITC, being forced to bring this lawsuit to stop Defendants' pattern of anticompetitive conduct, lost sales and business opportunities for EYLEA PFS, and developing a contingent source of EYLEA vials to guard against the risk that patients would not have access to EYLEA at all if Novartis succeeds in its efforts to block EYLEA PFS.

176. Competition in the anti-VEGF PFS market has been harmed by Novartis's monopolization attempts and its anticompetitive conspiracy with Vetter. Novartis, acting alone and in concert with Vetter, has delayed innovation and reduced patient choice in the anti-VEGF PFS market by resorting to every means possible to try to thwart the entry and sale of Regeneron's EYLEA PFS—a treatment regarded by many physicians as superior to LUCENTIS. Defendants have sought to deprive U.S. patients of a meaningful choice through their anticompetitive scheme that has as its heart Novartis's fraudulently procured '631 Patent. Novartis used that patent to bring Vetter under its dominion and to undermine the Vetter/Regeneron collaboration to develop and supply EYLEA PFS in the United States. Consistent with this scheme, Vetter attempted to leverage the then-pending application for the '631 Patent to extort a long-term supply agreement that would give Novartis and Vetter control over the supply of all anti-VEGF PFS treatments worldwide—including EYLEA PFS. When that failed, Vetter refused to provide any PFS filling services for EYLEA PFS, resulting in delay and significant expense to Regeneron to commercialize the product. And when EYLEA PFS finally launched to great success, Novartis filed suit to enforce the fraudulently procured '631 Patent to exclude EYLEA PFS from the market altogether, thereby

attempting to re-monopolize the market for anti-VEGF PFS treatments and deprive U.S. patients of the significant benefits of EYLEA PFS.

177. Defendants' anticompetitive conduct has forced Regeneron to divert precious and limited resources (which would otherwise be used for research and development to the benefit of patients) to navigate around the artificial and anticompetitive barriers that Defendants erected. Specifically, after being delayed by Novartis's and Vetter's anticompetitive exclusive licensing scheme, Regeneron was forced to spend additional substantial and unnecessary costs to develop a reliable supply of EYLEA PFS using a different filler, assembly lines, syringes, siliconization, sterilization, and PFS parts.

178. Now that Regeneron has finally developed its new supply and filler chain, obtained FDA approval, and launched EYLEA PFS in the United States, Regeneron is being forced to spend time and resources defending bogus litigation on multiple fronts based on a fraudulently procured patent. In addition, if Novartis succeeds, Regeneron will be forced to incur even more costs related to EYLEA PFS, such as attempting to secure an alternative domestic supply for PFS syringes (at significant time and expense) and obtaining the necessary regulatory approvals, and/or preparing for the possibility that EYLEA will be limited to vials. If Regeneron is forced to return its production and sales to EYLEA vials, it will incur substantial costs related to: (1) securing new sources of the required glass vials, stoppers, needles, containers, or other components; (2) identifying and negotiating vial filling capacity with third parties; (3) reserving contingent vial production capacity; (4) manufacturing additional bulk product for the contingent vial production; and (5) locating a new supplier or renegotiating with a current supplier to assemble the vial kits.

179. Most harmful of all, if Novartis succeeds in excluding EYLEA PFS, it will deprive patients and physicians of EYLEA in a more convenient and easier method of administration

altogether. By seeking to block EYLEA PFS from the U.S. market, Defendants are trying to force physicians to make a choice: choose the product regarded by many physicians and patients as superior—EYLEA (but in the significantly less preferred vial presentation)—or choose the more accurate and more convenient method of administration—LUCENTIS PFS (but with more frequent injections and lower efficacy for certain indications). The third option, Novartis's BEOVU, provides neither the safety of EYLEA nor the convenience of a PFS. Patients should not be forced to make this harmful tradeoff. Absent Defendants' anticompetitive conduct, physicians and patients could—and should—have all of these medical advantages combined into one treatment, Regeneron's EYLEA PFS.

180. With a monopoly over the U.S. anti-VEGF PFS market, Defendants also will have the power to increase prices to U.S. consumers. This is particularly harmful given that Regeneron has not materially increased the price of the EYLEA vial since its launch in 2011. Given that the only potential near-term entrant into the anti-VEGF PFS market is another treatment ***owned by Novartis*** (*i.e.*, BEOVU), Regeneron's EYLEA PFS places unique competitive pressures on LUCENTIS PFS. Novartis has admitted in its NDNY action that competition from EYLEA PFS has resulted and will continue to result in "a loss of market share, ***price erosion***, . . . and direct and indirect competition."[74] According to Novartis's own claims, therefore, the loss of EYLEA PFS will produce higher market shares and inflated prices for LUCENTIS PFS.

181. Lastly, Defendants' anticompetitive conduct sends a chilling message to any pharmaceutical company looking to invest in pioneering new and innovative anti-VEGF PFS treatments for ophthalmic diseases. Even if Regeneron prevails in the patent litigations brought by Novartis (as it fully expects to do), pharmaceutical companies seeking to engage in research and

[74] Novartis NDNY Compl. at ¶ 32.

development and enter the anti-VEGF PFS market will be deterred from doing so due to the prospect of significantly higher costs caused by Defendants' anticompetitive conduct, ultimately to the detriment of patients.

182. Novartis's and Vetter's unlawful conduct has accordingly deprived Regeneron, as well as patients and physicians, of the benefits of competition that the U.S. antitrust laws were designed to protect.

CLAIMS FOR RELIEF

COUNT ONE: ATTEMPTED MONOPOLIZATION THROUGH *WALKER PROCESS* FRAUD IN VIOLATION OF SECTION 2 OF THE SHERMAN ACT (against Novartis)

183. Regeneron incorporates by reference all of the allegations set forth above as if fully set forth below.

184. The '631 Patent is unenforceable because Novartis committed fraud on the USPTO in order to obtain the '631 Patent. At least three Novartis employees committed inequitable conduct, including Individual #1, a Novartis employee and the lead inventor of the '631 Patent, and Individual #2 and Individual #3, the Novartis patent practitioners responsible for the prosecution of the application that led to issuance of the '631 Patent (together, the "**Novartis Individuals**"). The Novartis Individuals knew of the prior art, knew that it was material, and deliberately withheld the existence of the prior art from the USPTO in order to obtain allowance of claims directed to a terminally sterilized anti-VEGF PFS.

185. The Novartis Individuals knew of material prior art that disclosed terminal sterilization of a PFS containing an anti-VEGF for intravitreal injection because of their involvement in the parallel prosecution (under a different set of examiners) of another Novartis application (the '380 Application) directed to terminal sterilization of a prefilled syringe. The Novartis Individuals also knew the information was material and deliberately withheld the

information demonstrating unpatentability from the Syringe Examiner evaluating the application for the ’631 Patent. More specifically, the Novartis Individuals deliberately withheld at least the following material information from the Syringe Examiner: (1) WO ’877; (2) Metzner; (3) Hasegawa; and (4) the five office actions from the Sterilization Examiners during the prosecution of the ’380 Application concluding that it was obvious to terminally sterilize a prefilled syringe containing an anti-VEGF drug product.

186. This information was material to the patentability of the claims of the ’631 Patent because the ’631 Patent would not have issued had the Syringe Examiner been aware of this undisclosed prior art and office actions by the Sterilization Examiners. The single most reasonable inference that may be drawn is that the Novartis Individuals withheld this material prior art with an intent to deceive the USPTO. The ’631 Patent issued to Novartis on December 29, 2015.

187. On June 19, 2020, Novartis filed multiple patent infringement actions against Regeneron, asserting the ’631 Patent in the ITC and NDNY, and seeking an exclusion order barring importation of EYLEA PFS and/or components thereof and other relief. Novartis asserted the ’631 Patent with full knowledge of the prosecution history of the ’631 Patent and the ’380 Application, and therefore with full knowledge of the fraudulent manner in which ’631 Patent was procured. The ITC and NDNY actions are an attempt by Novartis to hamper the introduction and expansion of Regeneron’s EYLEA PFS in the United States and to monopolize the anti-VEGF PFS market using the fraudulently procured ’631 Patent.

188. Anti-VEGFs in PFS that are approved by the FDA to treat certain ophthalmic diseases in the United States constitute a relevant market—the “anti-VEGF PFS market.”

189. Today, there are effectively only two such anti-VEGF PFS treatments approved in the United States: LUCENTIS PFS and EYLEA PFS.[75] Other products are not reasonable substitutes for, and not functionally interchangeable with, anti-VEGF PFS treatments because anti-VEGF PFS have unique characteristics, including superior efficacy and convenience, that distinguish them from alternative products, including anti-VEGFs supplied in vials. In response to a small but significant and non-transitory increase in the price of anti-VEGF PFS, U.S. physicians would not meaningfully switch their patients to any other product or treatment. Other practical indicia also support the conclusion that anti-VEGF PFS constitute the relevant product market.

190. The United States is the relevant geographic market for anti-VEGF PFS treatments. In order to be sold in the United States, anti-VEGF PFS products must be approved by the U.S. FDA, a process which is difficult, expensive, and time consuming. As a result, U.S. physicians cannot turn to products that are not approved for sale in the United States as an alternative, and would not be able to even if the price of U.S. anti-VEGF PFS products were to increase by a small, but significant and non-transitory amount.

191. From the time that LUCENTIS PFS launched in the United States in early 2017 until the recent commercial launch of EYLEA PFS, LUCENTIS PFS possessed monopoly power. During that period, LUCENTIS PFS was effectively the only available anti-VEGF PFS treatment with virtually 100% of the U.S. anti-VEGF PFS market. Although EYLEA PFS has launched, LUCENTIS PFS still retains a significant share of the U.S. anti-VEGF PFS market. LUCENTIS PFS' significant and durable market share is attributable to Novartis as the '631 Patent holder and licensor to Genentech, as well as the co-developer and co-owner of LUCENTIS and LUCENTIS

[75] While Macugen received FDA approval in 2004 for a prefilled syringe to treat wet AMD only, it is also an older, less effective treatment that is rarely prescribed anymore, if at all. Macugen is therefore not a competitive product in the anti-VEGF PFS market.

PFS. If Novartis succeeds in enjoining Regeneron's EYLEA PFS through its ITC action, then LUCENTIS PFS will automatically recapture virtually all or 100% of the anti-VEGF PFS market.

192. Significant and substantial commercial, developmental, regulatory, and other barriers insulate the anti-VEGF PFS market from new entry and expansion. Those barriers include, among other things, Novartis's fraudulently procured '631 Patent, which Novartis has used, and continues to use, in its unlawful attempts to exclude competition in the anti-VEGF PFS market.

193. Novartis's anticompetitive and exclusionary conduct has directly and proximately caused injury to Regeneron's business and property. As a result of Novartis's anticompetitive conduct, Regeneron has incurred, is incurring, or expects to incur, substantial costs and damages, including but not limited to, costs associated with: (1) defending against Novartis's unlawful ITC and NDNY actions; (2) invalidating Novartis's fraudulently procured '631 Patent; (3) securing alternative domestic sources of supply of PFS syringes and obtaining necessary regulatory approvals; and (4) preparing for the possibility that EYLEA will be limited to vial sales, including any and all costs relating to: (a) securing new sources of the required glass vials, stoppers, needles, containers, or other components; (b) identifying and negotiating vial filling capacity with third parties; (c) reserving contingent vial production capacity; (d) manufacturing additional bulk product for the contingent vial production; and (e) locating a new supplier or renegotiating with a current supplier to assemble the vial kits. Additionally, Regeneron may suffer a reduction in EYLEA sales due to the uncertainty that physicians will be able to continue prescribing EYLEA PFS.

194. Novartis's enforcement of its fraudulently procured '631 Patent constitutes anticompetitive conduct taken with the specific intent to monopolize the anti-VEGF PFS market in violation of Section 2 of the Sherman Act, 15 U.S.C. § 2. There is a dangerous probability that

Novartis will recapture its monopoly power. If Novartis succeeds in enforcing the '631 Patent and obtains an exclusion from the ITC, Novartis will eliminate EYLEA PFS from the U.S. market altogether, thereby restoring the LUCENTIS PFS monopoly with virtually all or 100% market share. Novartis admits that the launch of EYLEA PFS has caused Novartis to suffer "harm" that includes "loss of market share, price erosion,…and direct and indirect competition."[76] The "harms" that Novartis complains about are the very benefits of competition that the U.S. antitrust laws are designed to protect. Given that the only potential near-term entrant into the anti-VEGF PFS market is another drug owned by Novartis (*i.e.*, BEOVU), Regeneron's EYLEA PFS places unique competitive pressures on LUCENTIS PFS. If EYLEA PFS is foreclosed from the U.S. market, then LUCENTIS PFS will once again be the only anti-VEGF PFS drug approved by the FDA, enabling Novartis to control prices and exclude competition through its monopoly power.

195. Novartis's conduct has harmed competition by delaying innovation in the anti-VEGF PFS market, depriving U.S. physicians and patients of a meaningful choice and a preferred treatment, and reducing the availability of PFS ophthalmic disease treatments. Most harmful of all, if Novartis succeeds in its ITC action, it will deprive patients and physicians of EYLEA in a more convenient and easier method of administration altogether. Novartis is trying to force physicians to make a choice: choose the product regarded by many physicians and patients as superior—EYLEA (but in the significantly less preferred vial presentation)—or choose the more accurate and more convenient method of administration—LUCENTIS PFS (but with more frequent injections and lower efficacy for certain indications). The third option, Novartis's BEOVU, provides neither the safety of EYLEA nor the convenience of a PFS. Patients should not be forced to make this harmful tradeoff. Absent Novartis's anticompetitive conduct, physicians

[76] Novartis NDNY Compl. at ¶ 32.

and patients could—and should—have all of these medical advantages combined into one treatment, Regeneron's EYLEA PFS.

196. These injuries to Regeneron and to competition are of the type the antitrust laws are intended to prevent and flow directly from Novartis's anticompetitive conduct in violation of Section 2 of the Sherman Act.

197. Regeneron seeks injunctive relief, actual damages, trebled, plus interest, as well as attorneys' fees and costs under Sections 4 and 16 of the Clayton Act, 15 U.S.C. §§ 15 and 26.

COUNT TWO: ATTEMPTED MONOPOLIZATION IN VIOLATION OF SECTION 2 OF THE SHERMAN ACT (against Novartis)

198. Regeneron incorporates by reference all of the allegations set forth above as if fully set forth below.

199. Anti-VEGFs in PFS that are approved by the FDA to treat certain ophthalmic diseases in the United States constitute a relevant market—the "anti-VEGF PFS market."

200. Today, there are effectively only two such anti-VEGF PFS treatments approved in the United States: LUCENTIS PFS and EYLEA PFS.[77] Other products are not reasonable substitutes for, and not functionally interchangeable with, anti-VEGF PFS treatments because anti-VEGF PFS have unique characteristics, including superior accuracy and convenience, that distinguish them from alternative products, including anti-VEGFs supplied in vials. In response to a small but significant and non-transitory increase in the price of anti-VEGF PFS, U.S. physicians would not meaningfully switch their patients to any other product or treatment. Other practical indicia also support the conclusion that anti-VEGF PFS constitute a relevant product market.

201. The United States is the relevant geographic market for anti-VEGF PFS treatments.

[77] While Macugen received FDA approval in 2004 for a prefilled syringe to treat wet AMD only, it is also an older, less effective treatment that is rarely prescribed anymore, if at all. Macugen is therefore not a competitive product in the anti-VEGF PFS market.

In order to be sold in the United States, anti-VEGF PFS products must be approved by the U.S. FDA, a process which is difficult, expensive, and time consuming. As a result, U.S. physicians cannot turn to products that are not approved for sale in the United States as an alternative, and would not be able to even if the price of U.S. anti-VEGF PFS products were to increase by a small, but significant and non-transitory amount.

202. From the time that LUCENTIS PFS launched in the United States in early 2017 until the recent commercial launch of EYLEA PFS, LUCENTIS PFS possessed monopoly power. During that period, LUCENTIS PFS was the only available anti-VEGF PFS treatment with virtually 100% of the U.S. anti-VEGF PFS market. Although EYLEA PFS has launched, LUCENTIS PFS still retains a significant share of the U.S. anti-VEGF PFS market. LUCENTIS PFS' significant and durable market share is attributable to Novartis as the '631 Patent holder and licensor to Genentech, as well as the co-developer and co-owner of LUCENTIS and LUCENTIS PFS. Significant and substantial commercial, developmental, regulatory, and other barriers insulate the anti-VEGF PFS market from new entry and expansion.

203. Novartis embarked on an anticompetitive scheme to maintain, entrench, extend, and ultimately restore its monopoly power in the anti-VEGF PFS market, and the cornerstone of that scheme was Novartis's fraudulently procured '631 Patent. As described above, the '631 Patent is unenforceable because Novartis committed fraud on the USPTO. At least three Novartis employees committed inequitable conduct, including Individual #1, a Novartis employee and the lead inventor of the '631 Patent, and Individual #2 and Individual #3, the Novartis patent practitioners responsible for the prosecution of the application that led to issuance of the '631 Patent. These Novartis Individuals knew of the prior art, knew that it was material, and deliberately withheld the existence of the prior art from the USPTO in order to obtain allowance of claims

directed to a terminally sterilized anti-VEGF PFS. The single most reasonable inference that may be drawn is that the Novartis Individuals withheld this material prior art with an intent to deceive the USPTO. The '631 Patent issued to Novartis on December 29, 2015.

204. Novartis also attempted to monopolize the anti-VEGF PFS market by leveraging its fraudulently procured and unenforceable '631 Patent to coerce Regeneron into a 20-year exclusive PFS filler agreement with Vetter (Novartis's co-conspirator). In 2013, Novartis used the patent application that eventually became Novartis's fraudulently procured '631 Patent to obtain a lucrative economic interest in Vetter's PFS filling services in the form of Vetter's assent to encumber "existing customers"—notably Regeneron—with anticompetitive restrictions as a condition of continuing to work with them. Novartis effectively used the '631 Patent to obtain control over Vetter's filling customers and relationships. Following Novartis's anticompetitive agreement, Vetter demanded that Regeneron take a license to Novartis's pending patent application that later became the '631 Patent to continue developing EYLEA PFS. The catch was that Regeneron had to commit to a 20-year exclusive supply arrangement with Vetter for EYLEA PFS ***and*** agree never to challenge the enforceability of Novartis's fraudulently procured '631 Patent. Regeneron had no choice but to refuse.

205. The overarching goal of Novartis's monopolization scheme conduct was to control, and ultimately restrict, the supply of all anti-VEGF PFS treatments in the United States for nearly 20 years—*i.e.*, the duration of Novartis's unenforceable '631 Patent. By threatening Regeneron with infringement of the '631 Patent through Vetter, Novartis sought to delay competition from EYLEA PFS in order to maintain its LUCENTIS PFS monopoly as the only anti-VEGF PFS approved by the FDA in the United States. Alternatively, if Regeneron agreed to the exclusive EYLEA PFS filling relationship with Vetter, then Novartis would maintain its monopoly by

controlling, through its agreement with Vetter, the supply of all anti-VEGF PFS—LUCENTIS PFS, EYLEA PFS, and the new BEOVU PFS upon Novartis's commercial launch.

206. Now Novartis has taken the latest step in its monopolization scheme. On June 19, 2020, Novartis filed multiple bogus patent infringement lawsuits against Regeneron based on its fraudulently procured patent in the NDNY and ITC, seeking an exclusion order. Novartis has asserted the '631 Patent with full knowledge of the prosecution history of the '631 Patent and the '380 Application, and therefore with full knowledge of the fraudulent manner in which '631 Patent was procured. The NDNY and ITC actions are an attempt by Novartis to hamper the introduction and expansion of Regeneron's EYLEA PFS in the United States and to monopolize the anti-VEGF PFS market using a fraudulently procured patent.

207. Novartis's has acted with the specific intent to monopolize the anti-VEGF PFS market in violation of Section 2 of the Sherman Act, 15 U.S.C. § 2. Novartis's intent is evidenced by Novartis's anticompetitive conspiracy in Europe related to LUCENTIS, its attempts to stall and delay EYLEA PFS every step of the way through threats of patent infringement with Vetter, its attempts to hold EYLEA PFS captive to a 20-year filling arrangement so that it could limit supply, its efforts to mislead the public regarding the safety of BEOVU so as to steer patients away from EYLEA PFS, and finally its filing of bogus patent infringement lawsuits seeking to enjoin EYLEA PFS—conveniently timed right after its supposedly groundbreaking BEOVU crashed and burned in the United States.

208. There is a dangerous probability that Novartis will succeed in recapturing monopoly power through the enforcement of its fraudulently procured '631 Patent. If Novartis obtains an exclusion order from the ITC, then Novartis will eliminate EYLEA PFS from the U.S. market, thereby restoring the LUCENTIS PFS monopoly with virtually all or 100% market share.

Novartis admits that the launch of EYLEA PFS has caused Novartis to suffer "harm" that includes "loss of market share, price erosion,…and direct and indirect competition."[78] The "harms" that Novartis complains about are the very benefits of competition that the U.S. antitrust laws are designed to protect. Given that the only potential near-term entrant into the anti-VEGF PFS market is another drug owned by Novartis (*i.e.*, BEOVU), Regeneron's EYLEA PFS places unique competitive pressures on LUCENTIS PFS. If EYLEA PFS is foreclosed from the U.S. market, then LUCENTIS PFS will once again be the only anti-VEGF PFS drug approved by FDA, enabling Novartis to control prices and exclude competition through its monopoly power.

209. Novartis's anticompetitive and exclusionary conduct has directly and proximately caused injury to Regeneron's business and property. Regeneron has been forced to divert precious and limited resources (which would otherwise be used for research and development to the benefit of patients) to navigate around the artificial and anticompetitive barriers that Novartis erected. Specifically, Regeneron has incurred additional substantial and unnecessary costs, including for manufacturing and development, for its EYLEA PFS, spending years to develop an entirely new and alternative reliable supply of EYLEA PFS using a different filler, assembly lines, syringes, siliconization, terminal sterilization, and PFS parts.

210. Now that Regeneron has finally developed its new supply and filler chain, obtained FDA approval, and launched EYLEA PFS in the United States, Regeneron is being forced to spend time and resources defending bogus litigation on multiple fronts and invalidating Novartis's fraudulently procured '631 Patent. In addition, Regeneron will be forced to incur even more costs related to EYLEA PFS, such as securing alternative domestic supply for PFS syringes and obtaining the necessary regulatory approvals, and/or preparing for the possibility that EYLEA will

[78] Novartis NDNY Compl. at ¶ 32.

be limited to vials. If Regeneron is forced to return its production and sales to EYLEA vials, it will incur substantial costs related to: (1) securing new sources of the required glass vials, stoppers, needles, containers, or other components; (2) identifying and negotiating vial filling capacity with third parties; (3) reserving contingent vial production capacity; (4) manufacturing additional bulk product for the contingent vial production; and (5) locating a new supplier or renegotiating with a current supplier to assemble the vial kits. Additionally, Regeneron may suffer a reduction in EYLEA sales due to the uncertainty that physicians will be able to continue prescribing EYLEA PFS.

211. Novartis's conduct has harmed competition by delaying innovation in the anti-VEGF PFS market, depriving U.S. physicians and patients of a meaningful choice and a preferred treatment, and reducing the availability of PFS ophthalmic disease treatments. Most harmful of all, if Novartis succeeds in its ITC action, it will deprive patients and physicians of EYLEA in a more convenient and easier method of administration altogether. Novartis is trying to force physicians to make a choice: choose the product regarded by many physicians and patients as superior—EYLEA (but in the significantly less preferred vial presentation)—or choose the more accurate and more convenient method of administration—LUCENTIS PFS (but with more frequent injections and lower efficacy for certain indications). The third option, Novartis's BEOVU, provides neither the safety of EYLEA nor the convenience of a PFS. Patients should not be forced to make this harmful tradeoff. Absent Novartis's anticompetitive conduct, physicians and patients could—and should—have all of these medical advantages combined into one treatment, Regeneron's EYLEA PFS.

212. These injuries to Regeneron and to competition are of the type the antitrust laws are intended to prevent and flow directly from Novartis's anticompetitive conduct in violation of

Section 2 of the Sherman Act.

213. Regeneron seeks injunctive relief, actual damages, trebled, plus interest, as well as attorneys' fees and costs under Section 4 and 16 of the Clayton Act, 15 U.S.C. §§ 15 and 26.

COUNT THREE: UNREASONABLE RESTRAINT OF TRADE IN VIOLATION OF SECTION 1 OF THE SHERMAN ACT (against Novartis and Vetter)

214. Regeneron incorporates by reference all of the allegations set forth above as if fully set forth below.

215. Anti-VEGFs in PFS that are approved by the FDA to treat certain ophthalmic diseases in the United States constitute a relevant market—the "anti-VEGF PFS market."

216. Today, there are effectively only two such anti-VEGF PFS treatments approved in the United States: LUCENTIS PFS and EYLEA PFS.[79] Other products are not substitutes for, nor are they functionally interchangeable with, anti-VEGF PFS treatments because anti-VEGF PFS have unique characteristics, including superior accuracy and convenience, that distinguish them from alternative products, including anti-VEGFs supplied in vials. In response to a small but significant and non-transitory increase in the price of anti-VEGF PFS, U.S. physicians would not meaningfully switch their patients to any other product or treatment. Other practical indicia also support the conclusion that anti-VEGF PFS constitute the relevant product market.

217. The United States is the relevant geographic market for anti-VEGF PFS treatments. In order to be sold in the United States, anti-VEGF PFS products must be approved by the U.S. FDA, a process which is difficult, expensive, and time consuming. As a result, U.S. physicians cannot turn to products that are not approved for sale in the United States as an alternative, and would not be able to even if the price of U.S. anti-VEGF PFS products were to increase by a small,

[79] While Macugen received FDA approval in 2004 for a prefilled syringe to treat wet AMD only, it is also an older, less effective treatment that is rarely prescribed anymore, if at all. Macugen is therefore not a competitive product in the anti-VEGF PFS market.

but significant and non-transitory amount.

218. From the time that LUCENTIS PFS launched in the United States in early 2017 until the recent commercial launch of EYLEA PFS, LUCENTIS PFS possessed monopoly power. During that period, LUCENTIS PFS was the only available anti-VEGF PFS treatment approved by the FDA with virtually 100% of the U.S. anti-VEGF PFS market. Although EYLEA PFS has launched, LUCENTIS PFS retains market power in the U.S. anti-VEGF PFS market. LUCENTIS PFS' significant and durable market share is attributable to Novartis as the '631 Patent holder and licensor to Genentech, as well as the co-developer and co-owner of LUCENTIS and LUCENTIS PFS. If Novartis succeeds in enjoining Regeneron's EYLEA PFS through its ITC action, then LUCENTIS PFS will automatically recapture virtually all or 100% of the anti-VEGF PFS market. Significant and substantial commercial, developmental, regulatory, and other barriers insulate the anti-VEGF PFS market from new entry and expansion.

219. Shortly after Novartis submitted its application for what would become the fraudulently procured '631 Patent, Novartis embarked on a scheme to enlist Vetter in an anticompetitive conspiracy to hinder, delay, and unreasonably restrain competition in the PFS anti-VEGF market. Novartis and Vetter had been embroiled in an ownership dispute regarding the pending patent application, and Novartis used this settlement process to reach an anticompetitive arrangement with Vetter in 2013. While claiming to resolve a dispute over the '631 Patent, Defendants Novartis and Vetter entered into an unlawful conspiracy expressly aimed at controlling—and limiting—competition in the U.S. anti-VEGF PFS market.

220. Upon information and belief, Novartis provided Vetter with a "co-exclusive" license to its fraudulently procured '631 Patent in exchange for Novartis extracting a lucrative financial stake in Vetter's PFS filling services. This anticompetitive agreement co-opted Vetter,

allowing Novartis to exert influence over Vetter's current and future customer relationships. Novartis and Vetter agreed to certain undisclosed conditions regarding Vetter's existing customers including Regeneron. While Novartis would benefit from this anticompetitive agreement by controlling the entire anti-VEGF PFS market, Vetter would benefit by becoming the sole filler for the anti-VEGF PFS market—since Novartis would wield its '631 Patent against any company that tried to compete by using a different PFS filler. Novartis ultimately leveraged its fraudulently procured '631 Patent to secure Vetter's assent to disrupt the then-ongoing collaboration between Vetter and Regeneron to develop EYLEA PFS.

221. Following its anticompetitive agreement with Novartis, Vetter reversed course and did just as Novartis had planned. Despite having worked with Regeneron for approximately eight years on the development of EYLEA PFS, Vetter abruptly changed its conduct in late 2013, demanding that Regeneron take a sublicense to Novartis's patent application that later—in 2015—became the '631 Patent in order to continue development. Vetter then offered Regeneron a sublicense but with radically new and onerous terms. First, Regeneron had to agree to use Vetter as its exclusive PFS filler for the next 20 years—*i.e.*, throughout the life of Novartis's yet to be issued '631 Patent. Second, Regeneron had to agree never to challenge the validity or enforceability of Novartis's yet to be issued '631 Patent. The impact of this illicit "no-challenge" clause would have been to further cement Regeneron's exclusive filling arrangement with Vetter. It was designed to ensure that Regeneron could not use an alternative PFS filler under any circumstance, secured by the threat of an infringement action on a patent that Regeneron could not challenge.

222. Novartis and Vetter tried to leverage the fraudulently procured and unenforceable '631 Patent to coerce Regeneron into an exclusive arrangement with Vetter so that they could

control the supply of all anti-VEGF PFS drugs. The terms were carefully designed to ensure that any option Regeneron chose would accomplish the goal of limiting the competitive pressure from EYLEA PFS: either Vetter would force Regeneron to agree to the anticompetitive terms Novartis wanted and EYLEA PFS would be locked in as subordinate to LUCENTIS PFS with Vetter, or Regeneron would be forced to sever its relationship with Vetter, delaying the development and launch of EYLEA PFS and opening up Regeneron to vexatious litigation by Novartis under the fraudulently procured '631 Patent.

223. Regeneron was in a no-win situation. Regeneron either had to agree to Vetter's exclusive PFS filling agreement for 20 years, against its wishes, and accept a patent sublicense with a "no challenge" clause, or be forced to secure a completely new supply and fill chain for the EYLEA PFS and face a bogus infringement lawsuit. Regeneron ultimately had no choice but to reject Novartis's and Vetter's demands, even though it meant that the approval and launch of EYLEA PFS would be delayed significantly in the United States.

224. Following Regeneron's refusal to allow Vetter and Novartis to control the supply of all anti-VEGF PFS for nearly 20 years, Vetter refused to make its essential PFS filling services available to Regeneron for the EYLEA PFS. Given that Vetter is the dominant supplier of unique PFS filling services for anti-VEGFs and Vetter had been working with Regeneron for approximately eight years to develop EYLEA PFS, this unlawful joint conduct to deny Regeneron any non-exclusive PFS filling services ultimately harmed physicians, patients, and Regeneron. As a result of the Vetter-Novartis conspiracy and the significant market power flowing from that agreement, the onset of competition to LUCENTIS PFS was delayed by multiple years, leaving LUCENTIS PFS as effectively the only anti-VEGF PFS approved by the FDA on the market.

225. Novartis and Vetter did not stop there, however. They doubled down on their

anticompetitive conduct after the '631 Patent issued in December 2015. Vetter again demanded the same anticompetitive license terms from Regeneron in late 2017. Then, after Regeneron successfully created a new supply and filler chain for EYLEA PFS, and when BEOVU's serious safety problems came to light, Defendants took the next logical step in their conspiracy. Novartis sued Regeneron with its fraudulently procured '631 Patent on June 19, 2020, in the NDNY and also sought an exclusion order from ITC. Thus, despite knowing that the '631 Patent was fraudulently procured and unenforceable, Novartis filed multiple litigations in yet another attempt to block EYLEA PFS from the U.S. market altogether, or at the very least, to artificially increase Regeneron's costs even more by erecting anticompetitive barriers to sale.

226. Novartis and Vetter's anticompetitive and exclusionary conduct has directly and proximately caused injury to Regeneron's business and property. Regeneron has been forced to divert precious and limited resources (which would otherwise be used for research and development to the benefit of patients) to navigate around the artificial and anticompetitive barriers that Defendants erected. Specifically, Regeneron has incurred additional substantial and unnecessary costs, including for manufacturing and development, for its EYLEA PFS, spending years to develop an entirely new and alternative reliable supply of EYLEA PFS using a different filler, assembly lines, syringes, siliconization, terminal sterilization, and PFS parts.

227. Now that Regeneron has launched EYLEA PFS in the United States in competition with LUCENTIS PFS, Regeneron is being forced to spend time and resources defending bogus litigation on multiple fronts and invalidating Novartis's fraudulently procured '631 Patent. In addition, Regeneron will be forced to incur even more costs related to EYLEA PFS, such as securing alternative domestic supply for PFS syringes and obtaining the necessary regulatory approvals, and/or preparing for the possibility that EYLEA will be limited to vials. If Regeneron

is forced to return its production and sales to EYLEA vials, it will incur substantial costs related to: (1) securing new sources of the required glass vials, stoppers, needles, containers, or other components; (2) identifying and negotiating vial filling capacity with third parties; (3) reserving contingent vial production capacity; (4) manufacturing additional bulk product for the contingent vial production; and (5) locating a new supplier or renegotiating with a current supplier to assemble the vial kits. Additionally, Regeneron may suffer a reduction in EYLEA sales due to the uncertainty that physicians will be able to continue prescribing EYLEA PFS.

228. Novartis's and Vetter's anticompetitive conduct has harmed competition by delaying innovation in the anti-VEGF PFS market, depriving U.S. physicians and patients of a meaningful choice and a preferred treatment, and reducing the availability of PFS ophthalmic disease treatments. If Novartis succeeds in its ITC action, Defendants will eliminate EYLEA PFS from the U.S. market, thereby restoring the LUCENTIS PFS monopoly. Novartis admits that the U.S. launch of EYLEA PFS has caused it to suffer "harm" that includes "loss of market share, price erosion,…and direct and indirect competition."[80] The "harms" that Novartis complains of are the very benefits of competition that the U.S. antitrust laws are designed to protect. If EYLEA PFS is excluded, physician and patients will lose these benefits of competition, once again allowing Novartis to control prices and exclude rivals in the anti-VEGF PFS market.

229. Most harmful of all, Defendants will deprive patients and physicians of EYLEA in a more convenient and easier method of administration altogether. Defendants are trying to force physicians to make a choice: choose the product regarded by many physicians and patients as superior—EYLEA (but in the significantly less preferred vial presentation)—or choose the more accurate and more convenient method of administration—LUCENTIS PFS (but with more

[80] Novartis NDNY Compl. at ¶ 32.

frequent injections and lower efficacy for certain indications). The third option, Novartis's BEOVU, provides neither the safety of EYLEA nor the convenience of a PFS. Patients should not be forced to make this harmful tradeoff. Absent Defendants' anticompetitive conduct, physicians and patients could—and should—have all of these medical advantages combined into one treatment, Regeneron's EYLEA PFS.

230. These injuries to Regeneron and to competition are of the type the U.S. antitrust laws are intended to prevent and flow directly from Defendants' conduct in violation of Section 1 of the Sherman Act.

231. There is no procompetitive justification for the collusive agreement between Novartis and Vetter. This was no ordinary settlement of a patent ownership dispute between Novartis and Vetter as Novartis used it to acquire control over Vetter's filling customers and relationships. After collaborating with Regeneron for a long period of time, Vetter suddenly demanded exclusivity and, failing that, denied Regeneron access altogether to Vetter's unique PFS filling services for anti-VEGFs. Indeed, denying access had the effect of preventing and delaying Regeneron from obtaining PFS filling services necessary to compete against Novartis in selling an alternative, FDA-approved anti-VEGF PFS for the treatment of certain ophthalmic diseases.

232. Regeneron seeks injunctive relief, actual damages, trebled, plus interest, as well as attorneys' fees and costs under Sections 4 and 16 of the Clayton Act, 15 U.S.C. §§ 15 and 26.

PRAYER FOR RELIEF

WHEREFORE, Plaintiff Regeneron prays:

A. For judgment that:

(i) Defendants Novartis's and Vetter's conduct as stated in this Complaint violates Section 1 of the Sherman Act, 15 U.S.C. § 1;

(ii) Defendant Novartis's conduct as stated in this Complaint violates Section 2 of the Sherman Act, 15 U.S.C. § 2;

(iii) the '631 Patent be declared unenforceable;

B. For injunctive relief restraining and enjoining Defendants from continuing their unlawful conduct in violation of the Sherman Act;

C. That Defendants be required to pay to Plaintiff Regeneron:

(i) three times the actual damages sustained by Plaintiff as a result of Defendants' violations complained of herein;

(ii) Plaintiff's costs, disbursements, expenses, and reasonable attorneys' fees in bringing this action; and

D. For any such other relief that this Court deems just and proper.

JURY DEMAND

Pursuant to Federal Rule of Civil Procedure 38(b), Regeneron demands a trial by jury on all issues triable by jury.

Dated: July 17, 2020

New York, New York

By: */s/ Elizabeth Stotland Weiswasser*

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